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A Literature Review - Problem Definition Studies on Selected Toxic Chemicals

Volume 6 of 8

OCCUPATIONAL HEALTH AND SAFETY AND ENVIRONMENTAL
ASPECTS OF UREA-FORMALDEHYDE RESINS

Final Report - April, 1978

by

Shu-hsi Hsiao, Ph.D.

Principal Investigator

Jon E. Villaume, Ph.D.

Reviewed by

Frederick J. Goldstein, Ph.D.

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Project Officer

First Lt. Carl D. Rowlett, Medical Services Corps
Environmental Protection Research Division
U.S. Army Medical Bioengineering Research and Development Laboratory
Fort Detrick, Frederick, Maryland 21701

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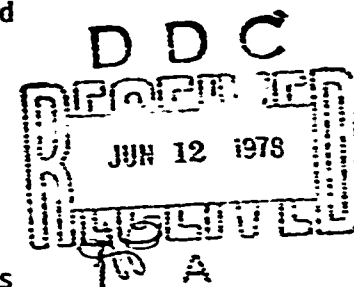
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The Problem Definition Study provides a literature review (88 references) on occupational health hazards and environmental impacts of urea-formaldehyde resins. This study covers the physical and chemical properties, toxicity in humans and animals, effects on microorganisms, plants, and soil organisms, pharmacokinetics, fate in the environment, industrial safety standards and practices and sampling and analysis of urea-formaldehyde resins. Environmental impacts are discussed and recommendations for further studies

19. KEY WORDS (Cont'd)

Microorganisms	Plants	Standards
Mutagenicity	Resins	Teratogenicity
Occurrence	Safety practices	TLV
Persistence	Sampling	Toxicity
Pharmacokinetics	Soil organisms	Transport
Physical properties		Urea-formaldehyde

20. ABSTRACT (Cont'd)

are provided. Urea-formaldehyde resins are mixtures of condensation products of urea and formaldehyde with indefinite composition, and structure depending on the degree of polymerization. The highly polymerized resins are inert solids which are very stable under ambient conditions and are not readily degraded in the environment. The low molecular weight condensation products are viscous liquids or powdery solids which decompose easily, releasing free formaldehyde that is highly irritating to eyes, skin and mucous membranes of humans and animals. They can be used as antibacterial products. If more urea than formaldehyde is present in the low molecular weight condensation products, they can be applied as fertilizers which are slowly degraded by soil microflora to release soluble nitrogen for growing plants. No reports on the effects of urea-formaldehyde resins on carcinogenesis, mutagenesis or teratogenesis were found in the literature, nor were reports on their effects on wildlife or aquatic organisms available. Although these resins are non-flammable, they do decompose under pyrolysis giving off toxic gases such as hydrogen cyanide, carbon monoxide, ammonia and carbon dioxide. There are no TLV or OSHA standards set for urea-formaldehyde resins in the workroom environment. Industrial safety practices involve the prevention of hazards caused by the release of formaldehyde. Special sampling and analytical methods are discussed.

EXECUTIVE SUMMARY

The literature review (88 references) discusses the occupational health and safety of urea-formaldehyde resins.

Urea-formaldehyde resins are thermosetting plastics used extensively in adhesive, molding, laminating, coating, insulation, textile and paper treatment. These resins are a mixture of condensation products of urea and formaldehyde. The composition and structure of these products depend on: a) conditions of the reaction, b) degree of polymerization, and c) molar ratio of the two components. The foam form of the resin is prepared by the interaction of urea and formaldehyde in the presence of a catalyst and a surfactant.

Low molecular weight products exist either as a water-soluble viscous liquid or a white powdery solid. These are converted by heat or acid into high polymeric forms which are water-insoluble amorphous solids. These two groups of resins will be discussed separately.

The high polymeric forms of the resins are colorless, transparent, odorless and tasteless solids, insoluble in cold water, cold dilute acids or alkalis. They are not affected by common organic solvents, oil or grease, but are decomposed in boiling water or in hot strong acids or alkalis. No studies on their effects on birds, aquatic organisms or wildlife are found in the literature. When the resins are ingested by animals, they are excreted in the feces without being metabolized. Since they are very stable under ambient conditions, accumulation in the environment is expected.

The low molecular weight condensation products, on the other hand, have quite different properties and effects. They are soluble in water and alcohol and decompose easily with the release of formaldehyde, which is the main cause of toxic effects.

Formaldehyde is highly irritating to eyes, skin, and mucous membrane. It is generated (1) during manufacture of the resins because it is one of the components, (2) during processing of the resins when heat is applied, such as molding, laminating, etc., (3) from resin products which contain incompletely reacted formaldehyde, and (4) from finished products which are not completely polymerized and decompose slowly to release formaldehyde.

Toxicity studies on urea-formaldehyde resins have focused upon the effects of formaldehyde which is generated as discussed above. Eye irritation was reported among factory workers and store employees where resin-treated fabrics were sold. Dermatoses developed among persons who came into direct contact with the resins, such as workers engaged in processing the resins and individuals wearing clothing made from resin-treated fabrics, which contain insufficiently polymerized resin.

1

The low molecular weight condensation products exert different effects on microorganisms depending on the proportion of urea and formaldehyde in the product. When the quantity of urea is less than that of formaldehyde, the product has antibacterial activity and has been used clinically to treat certain skin infections. When more urea is present than formaldehyde, the resulting product can be degraded by soil microorganism into soluble nitrogen compounds so that the product can be used as fertilizers.

In the environment the highly polymerized resins are stable to degradation under ordinary use-related conditions. Although they are non-flammable, they do decompose by incineration to release toxic gases such as hydrogen cyanide, carbon monoxide and ammonia. The low molecular weight condensation products are easily degraded chemically in hot water, dilute acid or alkaline solutions, and biologically by soil microflora.

No reports on carcinogenicity, mutagenicity, or teratogenicity of urea-formaldehyde resins were found in the literature. Neither are there any studies on the effects on aquatic organisms, birds, or wildlife.

There are no industrial threshold limit values for urea-formaldehyde resins. Safety practices involve mainly the prevention of hazards produced by formaldehyde, such as enclosed operations, adequate ventilation, cool room temperature, protective clothing and creams, personal hygiene, medical check-up, and education of workers.

Special methods for sampling and analysis of these resins are discussed.

Their impact on the environment is assessed and recommendations for further studies are provided.

2

ABSTRACT

The Problem Definition Study provides a literature review (88 references) on occupational health hazards and environmental impacts of urea-formaldehyde resins. This study covers the physical and chemical properties, toxicity in humans and animals, effects on microorganisms, plants, and soil organisms, pharmacokinetics, fate in the environment, industrial safety standards and practices and sampling and analysis of urea-formaldehyde resins. Environmental impacts are discussed and recommendations for further studies are provided. Urea-formaldehyde resins are mixtures of condensation products of urea and formaldehyde with indefinite composition, and structure depending on the degree of polymerization. The highly polymerized resins are inert solids which are very stable under ambient conditions and are not readily degraded in the environment. The low molecular weight condensation products are viscous liquids or powdery solids which decompose easily, releasing free formaldehyde that is highly irritating to eyes, skin and mucous membranes of humans and animals. They can be used as antibacterial products. If more urea than formaldehyde is present in the low molecular weight condensation products, they can be applied as fertilizers which are slowly degraded by soil microflora to release soluble nitrogen for growing plants. No reports on the effects of urea-formaldehyde resins on carcinogenesis, mutagenesis or teratogenesis were found in the literature, nor were reports on their effects on wildlife or aquatic organisms available. Although these resins are non-flammable, they do decompose under pyrolysis giving off toxic gases such as hydrogen cyanide, carbon monoxide, ammonia and carbon dioxide. There are no TLV or OSHA standards set for urea-formaldehyde resins in the workroom environment. Industrial safety practices involve the prevention of hazards caused by the release of formaldehyde. Special sampling and analytical methods are discussed.

3

FOREWORD

The industrial hygiene and occupational health research program of
the U. S. Army Medical Bioengineering Research and Development Laboratory,
Fort Detrick, Frederick, Maryland was initiated to study health problems and
recommend criteria for occupational exposure to military-unique chemicals.
This Problem Definition Study (PDS) has been prepared as part of the research
program under Contract Number DAMD-17-77-C-7020 in order to provide the
published data relating to occupational health and safety aspects and environ-
mental effects of urea-formaldehyde resins. These resins are mixtures of
condensation products of urea and formaldehyde. The subjects covered in
this report include physical and chemical properties, toxicity in humans
and animals, effects on plants, microorganisms and soil organisms, pharmaco-
kinetics, fate in the environment, industrial hygiene standards and safety
practices, sampling and analysis. Environmental impacts are discussed and
recommendations for further studies are provided.

TABLE OF CONTENTS

LIST OF TABLES

I. INTRODUCTION AND STATEMENT OF PROBLEM

The main objective of this study is to provide a literature review and an evaluation of the health hazards and environmental impacts of urea-formaldehyde resins.

Urea-formaldehyde resins are mixtures of condensation products of urea and formaldehyde; there is no single composition or structure. These resins are thermosetting plastics widely used in adhesives, surface coatings, molding of plastic objects, insulation, and textile and paper treatment. The present study provides a literature review covering physical and chemical properties, toxicity in humans and animals, effects on microorganisms and plants, pharmacokinetics, fate in the environment, sampling and analysis, industrial health hazards and safety standards. Environmental impacts will be discussed and recommendations for further studies will be given.

II. PHYSICAL AND CHEMICAL PROPERTIES

Urea-formaldehyde resins represent a group of condensation products of urea and formaldehyde for which there is no definite composition or structure. Depending on the conditions of the reaction (pH, temperature, catalysts, etc.) and the molar ratio of urea and formaldehyde, the condensation products may exist as a water-soluble viscous liquid, a white powder, or a colorless, transparent, amorphous resin. They belong to the class of thermosetting plastics because they are heat sensitive and thermofusible. When cured by heat or acid, condensation products are converted to higher polymeric forms which are hard, water-insoluble, nonflammable, heat and electric arc resistant. Various fillers and derivatives may be introduced into the resin to meet specific requirements. The physical and chemical properties of these resins will be discussed in the following section.

A. HISTORY

The reaction of urea and formaldehyde was first investigated by A. Hölzer (1884) and C. Goldschmidt (1896). During the 1920s, intensive studies were conducted in Europe to find use for the adhesive properties of the intermediate products and the inert quality of the cured final products of urea and form-aldehyde. Applications in molding, laminating, coating, insulating, and textile and paper treatment were investigated. The first commercial products appeared around 1930 (1-3). The chemical names, synonyms and trade names of urea-formaldehyde resins are listed in Table I.

B. PHYSICAL AND TECHNICAL PROPERTIES

The simple condensation products of urea and formaldehyde (the monomers and dimers) are viscous liquids which are soluble in water and in alcohol.

The intermediate products (polymers of moderate molecular weights) are amorphous powders soluble in pyridine, aqueous formaldehyde, formic acid, and dilute mineral acids (with some decomposition).

The cured final products are high molecular weight colorless transparent solids, which are insoluble in cold water and decomposed in boiling water. They are colorless and tasteless, and are relatively unaffected by common organic solvents, oils, greases, cold dilute acids or alkalis (but are decom-posed by hot acids or alkalis) (1-4). They do not discolor with time or light, but are affected by changes in humidity (contraction and expansion) because the final products contain a small percentage of water. The slow evaporation of this water with time also causes tiny cracks and slight distortion of the final products (1-3).

Various fillers, such as cellulose, wood flour, pigment, mineral, asbestos, glass fibers, etc., are added to the resins to reinforce their strength and improve their quality for molding purposes. Alcohol derivatives, especially n-butanol, are introduced to improve the solubility of the resins in non-aqueous solvents when they are used as surface coatings (1-3). The physical and technical properties of urea-formaldehyde resins are listed in Table II.

TABLE I

NAMES OF UREA-FORMALDEHYDE RESINS

Chem. Abs. Reg. No: 9011-05-6   Molecular formula $(CH_4N_2O,CH_2O)_x$

Systematic Name: Urea, Polymer with formaldehyde (Chemical Abstracts 9th C I)

Synonyms: Methylene-N,N'-bis(hydroxymethyl) urea polymer
                   urea-formaldehyde copolymer
                   urea-formaldehyde resin
                   urea-formaldehyde condensate
                   urea-formaldehyde precondensate
                   urea-formaldehyde primary condensate
                   urea-formaldehyde polymer
                   urea-formaldehyde prepolymer
                   urea-formaldehyde oligomer
                   urea-formaldehyde adduct
                   paraformaldehyde-urea resin
                   paraformaldehyde-urea polymer
                   formalin-urea copolymer
                   formaldehyde copolymer with urea
                   Uramite – DuPont, E. I. DeNemours & Co., Biochem. Dept.
                   Anaflex – Ed. Geistlish Söhne AC, Kolhusen, Switzerland.
                   Casco UL 30 – Borden Chem., Div. of Borden Inc.
                   Piatherm
                   Pianizol
                   Noxylin
                   Ponoxylan – Berk Pharmaceuticals, England
                   Polynoxylin
                   Hygromull – BASF, Germany
                   Mouldrite A256
                   K 411-02
                   MFPS-1
                   MF-1
                   MF
                   UKS-72
                   M-70

9

Table II.

Physical and Technical Properties of Urea-Formaldehyde Resins

Reference	1	2	3	5	6	7	7	8
Filler	a-cellulose	cellulose			a-cellulose	a-cellulose	Mineral	a-cellulose
Water absorption, 24 hrs, 25°C, %	0.4-0.8	0.75-2.0		0.75-3.0	0.4-0.8	up to 1.8	0.1-0.2	1.3
Specific gravity	1.47-1.52	1.5	1.48-1.52	1.45-1.55	1.48-1.52	~1.5	1.8-2.1	1.45-1.50
Flexural strength (psi)	$(10-16)\times10^3$	$(11-17)\times10^3$	$(10-16)\times10^3$	$(10-16)\times10^3$		~8 kgf/mm^2		$(10-13)\times10^3$
Impact strength, Izod (ft-lb)	0.25-0.4	0.24-0.28	0.26	0.24-0.36	0.26	0.2		0.28-0.32
Tensile strength (psi)	$(6-13)\times10^3$	$(5.5-7)\times10^3$	$(5-7)\times10^3$	$(6-13)\times10^3$	$(5-7)\times10^3$	~5 kg f/mm^2		$(5.5-7)\times10^3$
Compressive strength (psi)		$(3-3.8)\times10^4$	$(2.5-3.5)\times10^4$	$(2.4-3)\times10^4$		up to 30 kg f/mm^2		2.4×10^6
Modulus of Elasticity (psi)		$(1.4-1.5)\times10^6$		1.5×10^6	1.3	700-1000 kg f/mm^2	up to 2500	$(1.2-1.5)\times10^6$
Resistance to heat (°C)		77		82				77
Distortion under heat °C		127-138	132-138	127	130			127-138
Mold shrinkage	0.006-0.014	6-9 mils/in		0.005-0.011	0.005-0.008			0.006-0.011
Volume resistivity			10^{12}-10^{13}	10^{13}	10^{11}	10^{11}-10^{13}		10^{12}-10^{13}
Dielectric strength, 3/64" thick disc	300-400	330-370	300-400	650-720	330-370	12-18 kv/mm		650-720 (short time)
Dielectric strength, 1/8" thick disc				350-370				300-380 (stepwise)

10

Property					
Dielectric constant, 60 cycles	7.7-7.9	7.0-8.0	6.7-6.9	7.5 (50 Hz)	7.6-8.6
Dielectric constant, 10^6 cycles	6-8	6.4-7.5	6.7-6.9	6.5	6.6-7.7
Power factor, 60 cycles	0.025-0.035	0.035-0.045		0.03	0.04-0.055
" " 10^6 "		0.025-0.040		0.03	0.027-0.35
Loss factor, 60 cycles	0.28-0.36	0.24-0.36		0.3 (50 Hz)	
" " 10^6 "	0.19-0.21	0.16-0.30	0.19-0.21	0.05	
Arc resistance (seconds)	80-100	140	79-100		
Molding temperature °C	135-177		135-178		
Molding pressure (psi)	1-3 tons/in^2				compression 290-325
Rockwell hardness	M110-120	K94-97		K94-97 M110-125	M110-M120
Thermal expansion, per °C	$(2.2-3.0)\times10^{-5}$	$(7-10)\times10^{-4}$	$(2.2-3.6)\times10^{-5}$	$(2-5)\times10^{-5}$	$(2.5-3.0)\times10^{-5}$
Dissipation factor	0.025-0.035		0.029-0.091		
Boiling water test, 10 min, %	3.4	0.6		(30 min) up to 6	0.5 o.B.
Refractive index			1.54-1.56	~1.55	1.54-1.56
Compression ratio	2-3		2.5		2-3
Thermoconductivity, Cal/cm^2/sec/°C/cm			10.0×10^{-4}	~8	7.1×10^{-4}
Specific heat, cal/gm			0.4	0.4	0.4
Max. service temp, °C			76	75	
Elongation at break, %			0.75-1.0		
Insulation resistance, ohms	$(0.4-5.0)\times10^{10}$			$10^{11}-10^{12}$	
Annealing shrinkage, mils/in 48 hr, 105°C	6-12				

C.   CHEMISTRY AND MECHANISM OF REACTION

Commercially, these resins are prepared by condensing various proportions of urea and formalin (35-40% aqueous solution of formaldehyde) in slightly alkaline conditions.

The mechanism for the condensation of urea and formaldehyde is very complicated. There are various possible pathways by which the four replaceable hydrogen atoms of urea can react with formaldehyde to produce three dimensional structures. The properties of the final products are determined by a) the molar ratio of urea and formaldehyde, b) reaction pH and temperature, c) catalyst employed, and d) extent of condensation. When one mole of urea reacts with one or two moles of formaldehyde at "ordinary temperature" in slightly alkaline solutions (pH 7.5-11), white crystalline monomers are obtained which are soluble in water and melt at 111°C (for monomethylolurea) and 126°C (for dimethylolurea). The melting points for the monomers are not sharply defined because they tend to polymerize at high temperatures (110°-165°C) yielding amorphous substances which melt at 260°C with decomposition (1,2).

$$H_2NCNH_2 + HCHO \longrightarrow H_2NCNHCH_2OH \xrightarrow{HCHO} HOCH_2NHCNHCH_2OH$$

<center>monomethylolurea   dimethylolurea</center>
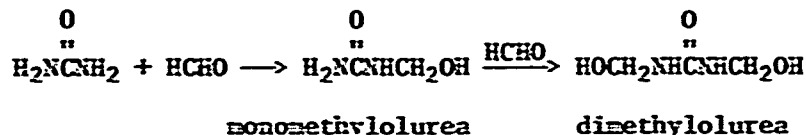
In acidic solutions, these methylolureas are converted to insoluble white granular deposits which are similar to the "Goldschmidt's compound" with the formula:

$$HOCH_2NHCNHCH_2OH \xrightarrow{-H_2O} H_2C=NCNHCH_2OH \longrightarrow [CH_2=NCNHCH_2NHCNHCH_2OH]$$

Further condensation by elimination of water probably proceeds through the following steps:

(1)   formation of methylene linkages,

$$-CNHCH_2OH + H_2NC- \xrightarrow{-H_2O} -CNHCH_2NHC-$$
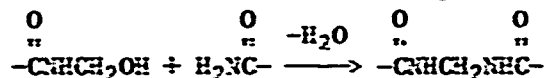
(2)   formation of methylene ether linkages,

$$-CNHCH_2OH + HOCH_2NHC- \xrightarrow{-H_2O} -CNHCH_2-O-CH_2NHC-$$
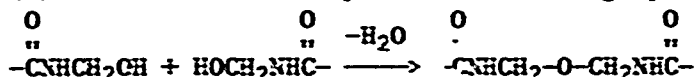
These intermediate products react with more formaldehyde or methylolureas to form branched-chain, cross-linked polymers which are insoluble and infusible. The curing process is accelerated by high temperature and acidic conditions (1,2).

The cured resins do not burn on free flame but crack and char with the odor of burned fish. Pyrolysis studies showed carbon dioxide, carbon monoxide and hydrogen cyanide are the major gaseous products (9-12).

III. HUMAN TOXICITY

In view of the literature available to date the completely cured urea-
formaldehyde resins do not appear to be toxic. However, during the manufacture
of these resins, one of the starting compounds, formaldehyde, is highly ir-
ritating to eyes, mucous membranes and skin. The other starting material,
urea, has not been shown to be toxic (1). The incompletely cured resins or
the low molecular weight condensation products may contain unreacted formalde-
hyde which could produce toxic symptoms. Under inefficient combustion con-
ditions these resins release toxic gaseous products, such as carbon monoxide,
hydrogen cyanide and ammonia, which may be the cause of death of some fire
victims (9,10).

Although urea formaldehyde resins are present in numerous products utilized
daily, very few cases of unpleasant reactions due to their employment have been
reported in the United States. The primary toxicity of these resins comes from
occupational contact of the starting material (formaldehyde vapor or the dust
of the low molecular weight condensation products) and the use of products con-
taining incompletely cured resins which release formaldehyde gradually. Most
of these incidents were reported outside of the United States. In the follow-
ing sections the effects of urea-formaldehyde resins on eye irritation, inhala-
tion and skin contact (dermatoses due to occupational contact and to use of
products) will be discussed. There are no reports on ill effects due to the
ingestion of these resins. Only a brief discussion on the effects of formal-
dehyde will be given below. A detailed toxicological report on formaldehyde
appears in a NIOSH criteria document (13).

A. EYE EXPOSURE

In Japan, Tojo and Tsuji reported two cases of lacrimal sensitivity to
imported synthetic materials (14). A 52-year-old woman and her 19-year-old
daughter experienced excessive lacrimation whenever they were in a shop sell-
ing synthetic fabrics. The gaseous material responsible for this effect was
found to be formaldehyde which was released from fabrics treated with formal-
dehyde resins to improve their wrinkle and shrink resistance and water repel-
lency. The incompletely reacted formaldehyde, and/or that produced from de-
composition of the resin, were released gradually from the treated fabrics,
thus causing extreme lacrimation in exposed individuals. Employees of
fabric stores were constantly affected by these fumes and loss of customers
was reported (15).

B. INHALATION

Volkova and Sidorova detected formaldehyde in the blood of 100 workers
who were exposed to urea-formaldehyde or melamine-formaldehyde resins (16).
It was present in the blood 15-70 minutes after work and disappeared in
18 hours. Blood levels of formaldehyde were directly related to that in the
air. It was also detected on the skin and clothing of workers exposed to high
concentrations of formaldehyde in the air.

Female workers exposed to various concentrations of formaldehyde from
urea-formaldehyde resins were reported to suffer ill effects (17). Menstrual

13

disorders, such as dysmenorrhea, were recorded 2 1/2 times as often as in the controls. There were also complications in the course of pregnancy, such as toxemias, anemia, and interruptions at different terms of pregnancy. From this group of workers, 26.9% of the children were born underweight (from 2500 to 3000 g) as compared to 11.3% in controls.

C.   SKIN CONTACT

1.   OCCUPATIONAL DERMATOSES

In 1936, Schwartz reported many cases of dermatitis due to hypersensitivity to formaldehyde among workers manufacturing urea-formaldehyde resins (18,19). In two factories surveyed, where modern machinery and safety appliances with adequate ventilation and dust prevention facilities were installed, only four cases of dermatitis were reported among 190 employees during a period of over two years. In contrast, 26 cases of dermatitis occurred in the first 10 months of 1934 among 300 workers in a molding plant in Ohio; 18 of these cases occurring during the hot summer months. The effect of high ambient temperature and inadequate ventilation was also apparent when half of the workers (number not given) employed in a molding plant in Pennsylvania developed dermatitis in the summer of 1935.

The Michigan Department of Health of the Bureau of Industrial Hygiene reported a severe outbreak of dermatitis in 1943 due to exposure to formaldehyde resins (including phenol-, urea- and melamine-formaldehyde resins) (20). The study involved 4 factories in Western Michigan employing 2,370 workers, 355 of which developed dermatitis; many severe cases (numbers not given) required hospitalization. The onset of dermatitis occurred from 3-6 weeks after initial exposure to the formaldehyde resins and lasted from several days to a few months. Some individuals may have developed immunity after initial exposure and did not react to formaldehyde on subsequent contact. Should these individuals later lose their immunity, a severe case of dermatitis might ensue (20).

Outside of the United States, most of the occupational dermatosis cases were reported in the Soviet Union (16,17,21-25) and a few in other countries (26-29). In a factory producing veneer, examination of 198 workers showed dermatoses in those who had been working with liquid resins for 1-3 months (21). Local treatment with an ointment containing zinc (% not available) and 0.5% prednisolone eliminated the condition in 7-10 days. Frequent washing of the exposed skin with 0.5% ammonium hydroxide solution reduced the incidence of dermatoses. The quantity of formaldehyde in the resin could also be lowered to 0.5-1.0% by the addition of ammonium hydroxide to the resin (21).

In two large furniture plants a high incidence of dermatoses was reported (22). The greatest effect was produced by a) resins in a pure state, b) formalin and c) polyether varnishes. The authors suggested preliminary medical examinations of newly engaged workers using specific tests, and monthly examinations during the first 6 months of work. They also suggested that a section be included in manuals on the unhealthy conditions in furniture plants where urea-formaldehyde resins were used, in order to instruct the workers in the proper hygienic and safety practices.

14

El-Sayad claimed that the skin sensitizing action of urea-formaldehyde resins was not due to the high concentrations of free formaldehyde, but mainly to the polycondensation products (23). A clinical investigation of the sensitizing effects of pure formaldehyde solution, polymeric condensation products, and monomers on 74 patients who suffered occupational dermatosis showed that phenol-formaldehyde resins had greater skin sensitizing effects than urea-formaldehyde resins. The author concluded that allergic dermatosis was caused by the resins and not by free formaldehyde. Presence of the latter could increase the probability of the occurrence of dermatosis, but formaldehyde itself did not produce the allergenic effect.

During a dermatological examination of 33 women workers exposed to synthetic binders while making glass-wool cylinders, 21 cases of pruriginous skin diseases, 9 cases of eczema and 13 cases of dry skin and slight erythema were reported (24). The synthetic binder consisted of urea-formaldehyde resins modified with vinyl derivatices and contained 0.5% free formaldehyde. Sensitization developed after 3-4 months on the job; the condition was enhanced by skin injuries caused by the glass-wool.

Other cases of occupational dermatoses have been reported in persons working with resins for processing noncrushable fabrics (26,27), for coating anticurl substances (28), and for applying glue on toilet rolls (29).

2. DERMATOSES IN USERS OF UREA-FORMALDEHYDE PRODUCTS

In addition to the dermatoses caused by occupational contact of urea-formaldehyde condensation products, there were many cases of skin irritation (mostly reported outside of the United States) due to the use of products that had been treated with urea-formaldehyde resins to improve their qualities, such as "wet strength" facial tissues, and non-shrinkable fabrics that are water-repellent and wrinkle-resistant. The main cause of trouble was due to the incompletely cured resin remaining in fabrics which were not thoroughly washed before being sent to the market. The residual formaldehyde would cause skin irritation and dermatoses in people wearing clothing made from these treated fabrics. Such cases will be discussed in detail.

Sensitization to "wet strength" facial tissues impregnated with urea-formaldehyde resins was studied by Peck and Palitz (30). The amount of resins applied to the tissue is usually less than 2%, but the temperature required for complete cure of the resins is so high that very few paper machines are equipped to produce completely cured tissue. The formaldehyde from the incompletely cured resin can produce dermatitis in individuals sensitive to it. A patch test on 50 people (15 males; 35 females) with "wet strength" tissue on one arm, and another tissue without any additive on the other arm showed that 6% of the people tested (3 out of 50 - 2 female; 1 male) had sensitive reactions to the treated tissues. No reactions were observed from tissues that did not contain additives.

Since the introduction of resin-treated textiles in 1926, only a few cases of contact dermatoses due to the use of these fabrics have been reported within the United States (31,32,33), although many cases were reported in European countries (15,34,35). An early report was made in 1940 by Schwartz

15

of the United States Public Health Service after an outbreak of dermatitis
among the general population of the United States and Canada caused by wearing
clothing made from such treated fabrics (31). The odor of formaldehyde was
readily detectable from these fabrics and its concentration was found to be
8-100 mg/100 g yarn. The author suggested that manufacturers should perform
skin tests on animals and humans before sending the products to the market.
In addition, treating these fabrics at higher temperature and pressure to com-
plete the curing process, and thorough washing of the finished product would
also reduce the concentration of free formaldehyde.

Fisher et al. investigated the problem by (1) detecting the presence of
free formaldehyde in textiles, (2) making patch tests on humans with samples
of suspected fabrics, and (3) having subjects wear clothes made from these
fabrics (36). It was found that all samples of textiles treated with formal-
dehyde resins gave positive reaction with the qualititive chromotropic acid
test (see section on analysis). Control samples of untreated textiles showed
negative reactions. Patch tests on 20 patients (8 males; 12 females), who
previously gave positive reactions with 2-5% formaldehyde solutions (as patch
tests), showed negative results with 8 treated textile samples containing
varying amounts of free formaldehyde. None of these formaldehyde sensitive
individuals developed dermatitis after wearing clothing made from these treated
fabrics. The authors concluded that the quantity of free formaldehyde in the
test materials was not sufficient to elicit a positive patch test in individuals
who reacted to 2-5% formaldehyde solutions. By applying similar methods of
investigation, a few cases of contact dermatoses due to resin treated fabrics
have been studied (32,33).

Outside of the United States, many cases of contact eczema and dermatitis
caused by the formaldehyde from treated textiles have been reported. In Norway,
a patch test was conducted on 2,110 patients during 1953-1958, and 137 (6.5%
average - 3.56% for males and 9.04% for females) were found sensitive to 4%
aqueous formaldehyde (15). Of these 137 patients with positive reactions,
69 of them (24 males; 45 females) had formaldehyde eczema; the remaining 68
(27 males and 41 females) showed no significant clinical symptoms (15). Since
more women than men reacted to formaldehyde and to the treated fabrics, the
author suggested that women might have been sensitized to the formaldehyde
included in antiperspirant preparations which men used less extensively than
women. This may also be the reason for the paucity of contact dermatoses
in the United States because formaldehyde is not used in antiperspirants in
this country.

A study conducted in Denmark showed that during 1952-1960 the incidence
of formaldehyde eczema due t treated fabrics had been rising whereas that
caused by antiperspirants had disappeared (34). In 1960, formaldehyde in
treated fabrics was responsible for 50% of the contact dermatoses in Denmark
because even small amounts of free formaldehyde in the fabric can elicit
dermatitis in persons already sensitized by prior utilization of antiperspir-
ants. A simple screening test was used on 96 patients (30 male; 66 female);
35 (5 males; 30 females) showed positive reactions with treated textiles (34).
In the Netherlands, a patch test was conducted on 66 patients with 37 sub-
stances (including urea-formaldehyde condensation products) used in treating
textiles. Only 7 patients reacted positively to formaldehyde, having been
sensitized previously.

16

IV. EFFECTS ON EXPERIMENTAL ANIMALS

There are only a few reports in the literature describing animal experiments on the toxicity of urea-formaldehyde resins. The completely cured resins are generally considered to be nontoxic (7,37). The adverse effects of the urea-formaldehyde resins on animals are apparently due to the presence of free formaldehyde. It should be kept in mind that the products used for the experiments discussed in this report vary in their composition and free formaldehyde content which greatly influences the effects of these resins. A summary of these studies appears in Table III.

A. ORAL INGESTION

The acute oral toxicity of a condensation product of urea and formaldehyde (trade name, Anaflex, manufactured by Ed. Geistlich Söhne AG, Wolhusen, Switzerland) was determined in guinea pigs (37). The substance was administered in the form of tablets (inserted down the esophagus) to 6 groups of animals (5 per group) at single doses of 480–2320 mg/kg of body weight. All animals survived without any pathological changes during the test itself and the 8-day observation period.

The subchronic toxicity of the same product was determined using rats (strain, sex, age and number not given) given daily doses, for 9 weeks, of 1 g/kg body weight in the form of a 20% polysorbate solution administered with a pharyngeal tube. Histological examination of the rats did not reveal abnormalities in the intestinal tract, liver or kidneys (37).

Urea-formaldehyde resins were given to albino rats by gavage at 5 g/kg every other day for 6 days (3 doses). Fifty rats were used to test 5 plastic materials but the number given urea-formaldehyde was not specified. No toxic effects were observed. There were no changes in weight gain, in the nervous system (central or peripheral not specified), or in the blood picture. Additional details were not provided (38).

The effects of oral administration of a commercial preparation of urea-formaldehyde resin, Uramite, as a non-protein nitrogen source in animal feed, were studied by Anderson et al. (39). Grade Hampshire wether lambs (average weight 29.25 kg, 2 per group) were fed diets containing 2%, 4%, 8%, 16% or 32% of Uramite, plus a sufficient percent of urea to equal 100% supplementary non-protein nitrogen. The maximum amount of feed which would be consumed completely by all the lambs was established during an adjustment period (duration not given). The lambs were then fed the rations at the previously established levels. The collection period began after all animals had consistently consumed their entire ration for 10 consecutive days. Daily excreta were collected for 10 days and analyzed for nitrogen output. Results showed that much of the nitrogen in Uramite was excreted in the feces. The replacement of 4–32% of urea by Uramite reduced the digestibility of crude protein (p<0.05), and 2–4% of Uramite reduced the digestibility of crude fiber (p<0.01). No toxic effects were observed (39).

17

B. DERMAL APPLICATION

Two types of urea-formaldehyde resins (MF-17, 29% free formaldehyde, pH 8.3; UKS, 1.2% free formaldehyde, pH 9) (specific formulation not given) were studied for dermal effects on 10 albino guinea pigs (300-350 g). The resins were applied on the skin by the compress method on one occasion and repeatedly by simple application (duration not given). The MF-17 resin caused erythema, dryness of the skin, desquamation and superficial cracks in 7 out of 10 animals. Three animals were found sensitized on the 25th day. The UKS resin caused erythema in 3 out of 10 animals on the 4th day; 8 out of 10 animals showed skin irritation on the 11th day. The two resins contained different quantities of free formaldehyde but produced similar degrees of irritation. The author concluded that the sensitizing effect is not due to free formaldehyde (23).

Lumps of urea-formaldehyde resins were applied to the skin of 4 rabbits, 4 hours a day for 4 days. No cutaneous changes were observed. Additional details were not provided (38).

C. INHALATION

When urea-formaldehyde resin (80-85 g) was heated at 55-65°, no measurable quantity of urea was released. Rats (number not given) were exposed to the volatile components (diluted to 100 liters) 2 hours per day for 12 days. No toxic effects were observed (38). The report did not mention whether free formaldehyde was released or how the rats were exposed.

The toxicity of the gaseous products released by combustion of urea-formaldehyde resin was tested with Sprague-Dawley rats (2 controls and 2 treated). The combustion effluent was generated by heating the resin at 1100°C. The effluent was kept above the dew point to prevent condensation and adjusted to 24°C and 50% humidity with cool dry air before entering the exposure chamber. Rats exposed to the effluent (duration not given) suffered eye irritation and "heavy" breathing. Gross symptoms disappeared within a week after exposure.

D. EYE APPLICATION

When powdered urea-formaldehyde resin was introduced into the conjunctival sac of 4 rabbits (duration not given), the resin powder caused transient lacrimation but no inflammation (38).

TABLE III

TOXICOLOGICAL STUDIES IN EXPERIMENTAL ANIMALS

Species (Number)	Route	Formulation	Dose and Duration	Results	Reference
Guinea pigs (5/grp)	Oral	Anaflex-condensation product of urea and formaldehyde.	480-2320 mg/kg single dose	No effects	(37)
Rats (NR)	Oral	Urea-formaldehyde resins	3 x 5 g/kg every other day for 6 days	No effects	(37)
Lambs (2/grp)	Oral	Uramite-as nitrogen supplement in feed	2-32% in diet for 10 days	No effects	(39)
Rats (NR)	Oral	Anaflex-condensation product of urea and formaldehyde	1 g/kg daily for 9 weeks	No effects	(37)
Guinea pigs (10)	Dermal	MF-17- 29% formaldehyde	NR NR	Erythema, dryness of the skin, desquamation, superficial cracks in 7/10 by day 25	(23)
Guinea pigs (10)	Dermal	UFS - 1.2% formaldehyde	NR NR	Erythema in 3/10 by day 4 and in 5/10 by day 11	(23)
Rabbits (4)	Dermal	"lumps" of resin	NR 4 hr/day for 4 days	No effects	(38)
Rats (4)	Inhalation	Gaseous products from combustion of resin	NR NR	Eye irritation "Heavy" breathing	(10)
Rats (10)	Inhalation	Volatile components from heated resin diluted to 100 liters	NR 2 hr/day for 12 days	No effects	(38)
Rabbits (4)	Topical: eye	Resin powder inserted into conjunctival sac	NR NR	Transient lacrimation; no inflammation	(38)

NR - not reported

V. CARCINOGENICITY, MUTAGENICITY AND TERATOGENICITY

No reports on carcinogenicity, mutagenicity or teratogenicity of urea-formaldehyde resins were found in the literature.

VI. EFFECTS ON DOMESTIC ANIMALS AND WILDLIFE

There are no reports in the collected literature concerning the effects of urea-formaldehyde resins on domestic animals or wildlife. For urea-formaldehyde metabolism in lambs, see Chapter XI.

VII. EFFECTS ON AQUATIC ORGANISMS

No studies on the effects of urea-formaldehyde resins on aquatic organisms are available.

VIII. EFFECTS ON MICROORGANISMS

The completely cured urea-formaldehyde resins in highly polymerized forms have no apparent effects on microorganisms nor do microorganisms attack the resins (40). The effects of low molecular weight condensation products on microorganisms depend on the molar ratio of urea (U) and formaldehyde (F). When the ratio is less than unity (U/F < 1) the excess formaldehyde in the resins exert an antibacterial effect which has been applied clinically to treat certain skin infections. When the molar ratio is greater than one (U/F > 1), the cured resins can be used as fertilizers because soil micro-organisms can attack and break down these products to provide a nitrogen source for growing plants (see Biological Degradation). The antibacterial and anti-fungal effects of urea-formaldehyde resins are as follows.

The bacteriostatic action of the condensation products of urea and formaldehyde was first reported by Brodhage and Stofer (37). A product pre-pared by a modified process under the trade name of Anaflex (Ed. Geistlich Söhne AG, Wolhusen, Switzerland) is a colorless powder, insoluble in water, and decomposes at 200°C. The bacteriostatic action of the pure sub-stance was tested on blood-agar plates inoculated with 9 strains of bacteria. After 16-18 hours of incubation, the diameters of the inhibition zones caused by 10-25 mg of the substance were: 26-32 mm for *Staphylococcus aureus hemo-lyticus*, 30-48 mm for *Streptococcus pyogenes hemolyticus*, 19-29 mm for *Strepto-coccus faecalis*, 26-35 mm for *Salmonella paratyphi* B, 29-40 mm for *Salmonella typhi*, 15-19 mm for *Pseudomonas aeruginosa*, 23-35 mm for *Proteus vulgaris*, 15-20 mm for *Escherichia coli*; and 25-28 mm for *Listeria monocytogenes*. The diameter of the powder spread was 8-10 mm. The authors concluded that Anaflex had good bacteriostatic action in vitro against gram-negative and gram-positive bacteria (37).

Since many strains of *Staphylococcus* are resistant to antibiotics, the bacteriostatic effect of this product was tested on six "distinct" *Staphylo-coccus* strains. The results show that the effect *in vitro* is dependent on the antibiotic resistance of the *Staphylococcus* strains individually (data not given) (37).

Haler showed that Anaflex or polynoxylin, prepared by curing the water-soluble condensate of urea and formaldehyde at alkaline pH, exhibits broad-spectrum bacteriostatic properties (41,42). This is different from condensation products of urea and formaldehyde cured with acid reagents at either high or low temperature which do not show any bacteriostatic activity (41). The tests were carried out by Fleming's disk and ditch methods because of the low solubility in water of the product. Tests in liquid media were made with 1% suspensions of the test material .

A total of 37 species (580 strains) of bacteria and fungi were tested: these were 125 strains of *Staphylococcus aureus*, 59 of *Streptococcus pyogenes*, 210 of *Escherichia coli*, 82 of *Proteus vulgaris*, 39 of *Pseudomonas aeruginosa*, 18 of *Candida albicans*, 24 of *Epidermophyton floccosum*, and 23 of *Trichophyton* spp. All (except 3 strains of *Pseudomonas aeruginosa* and 3 strains of *Candida albicans*) were found sensitive to Anaflex, including those strains of *Staphylo-coccus aureus* resistant to penicillin, tetracycline, and other antibiotics. No resistance of *Staphylococcus aureus*, *Streptococcus pyogenes* or *Pseudomonas*

21

aeruginosa against Anaflex could be induced by repeated sub-culturing up to 160 passages. Water was found essential for the bacteriostatic activity of Anaflex. The presence of serum, blood or pus in the agar also increased the inhibition zones of *Staphylococcus aureus*. Viruses of herpes simplex, vaccinia and poliomyelitis, however, were not sensitive to Anaflex (42).

The antibacterial effect of polynoxylin was tested with 170 strains of *Proteus vulgaris, Proteus morganii, Salmonella typhosa, Klebsiella pneumoniae, Pseudomonas aeruginosa, Streptococcus faecalis, Staphylococcus aureus, Streptococcus pyogenes, Escherichia coli, Aerobactor aerogenes,* and *Aerobacter cloacae* on solid media. Standard antibiotics, such as penicillin, streptomycin, chloramphenicol, tetracycline, erythromycin, neomycin, polymyxin, chlortetracycline, oxytetracycline, novobiocin and albomycin, were also tested on these strains of bacteria for comparison. Polynoxylin was effective against all strains tested except a strain of *Aerobacter cloacae*. The inhibitory effect of polynoxylin was most pronounced against *Staphylococcus aureus*, less against *Proteus vulgaris* and *Streptococcus faecalis*, and least against *Escherichia coli* and *Aerobacter aerogenes* but still within the range of therapeutic doses. Strains of *Staphylococcus aureus* resistant to antibiotics were less inhibited by polynoxylin than those susceptible to antibiotics in this study, in contrast with previous findings (41).

The antibacterial and antifungal activities of Anaflex were clinically tested on more than 200 human patients representing 238 cases of furunculosis, ulcus cruris, infected acne, pressure sores and industrial wounds, gynecological discharges, fungal paronychia, athlete's foot, cutaneous hypersensitivity, axilliary infections, seborrhea capitis, napkin rash and proctological cases. The product was applied directly to the affected part twice daily and also as a ring around the area to minimize secondary spread. Although not all the patients treated were cured (results not given), more than 80% of the furunculosis cases were cured in less than 4 days. If the initial lesions were treated within 48 hours they disappeared in 2 days and classical boils were avoided. A nasal barrier cream containing Anaflex removed the infection of penicillin-resistant *Staphylococcus* within 4-5 days. Relapses to the carrier state took 7 days or more. A commercial cream containing chlorhexidine produced a similar effect in 2-3 days, but relapse occurred in 3 days (41).

Clinical experience from topical application of urea-formaldehyde condensation products (Anaflex) for treatment of some skin diseases was also reported by Tomasini in Italy (43). From a total of 114 cases (74 males; 40 females) tested, the results were satisfactory in general and the products were found most effective in treating mycotic and pyogenic dermatitis.

Utilization of antibacterial properties of urea-formaldehyde condensation products to treat raw sewage and industrial organic waste materials in order to kill pathological microbes and render the waste reusable has been proposed (44). The process involves prereacting the waste with a water-soluble low condensation product of urea and formaldehyde at pH 7-9 to sterilize the waste, then acidifying the mixture to pH 3-5 for further condensation to take place, and finally neutralizing and drying the product which can then be used as fertilizer or animal feed.

22

Kingston measured the formaldehyde liberated into the vapor phase from Anaflex and Noxythiolin (a condensation product of thiourea and formaldehyde) (45). Two small beakers, one containing the dry product (0.1 g), the other, 0.5 ml of distilled water were placed in a jar. The jar was tightly sealed and incubated at 37°C for various periods of time. The formaldehyde vapor released by the dry product was absorbed by the water which was analyzed colorimetrically by the method of Nash. From 0.1 g of the dry product, 1-2 mg of formaldehyde vapor was collected from Noxythiolin and only 0.2 mg from Anaflex. When the latter was wetted with 1 ml of water, less formaldehyde was released in the vapor phase but 1.5 mg of it was detected in the supernatant. The bacteriostatic activity of Noxythiolin (1 mg) was compared with that of formaldehyde (0.2 mg) on agar plate tests with 3 organisms. The inhibition zones produced by formaldehyde were comparable in size with those obtained with Noxythiolin. The author concluded that the free formaldehyde released by Noxythiolin is the cause of the bacteriostatic effects. Formaldehyde slowly released by Anaflex may be bacteriostatic but tests are inconclusive (45).

Although it was assumed that the mechanism of the antibacterial action of Anaflex was due to free formaldehyde in the product, Haler found that a negative reaction with Schiff's aldehyde reagent was obtained when the product was shaken with water for prolonged periods (42). A water-soluble condensate of urea and formaldehyde also gave negative reactions for formaldehyde, but when tested with Schiff's reagent in excess acid, a strong positive reaction with precipitates was obtained. When this modified test was conducted on Anaflex and its aqueous filtrate an immediate positive reaction was obtained with older stocks, and delayed reaction with fresh stocks. The observation that the positive aldehyde test was not due to free formaldehyde was further confirmed with a rabbit and a human volunteer which were both hypersensitive to formaldehyde. The subcutaneous injection of 0.05% formalin (0.2 ml) in the rabbit produced a marked local reaction within 5 minutes and a severe generalized reaction after 65 minutes. No local or systemic reactions were observed when a saturated solution of Anaflex was administered to rabbit subcutaneously, 0.2 ml daily for 4 days followed by daily injections of 0.3, 0.4, and 0.5 ml for 3 days, respectively. These results are questionable, however, since only one animal was used. The human volunteer developed an edematous reaction after contact with very dilute formaldehyde but showed only a very slight degree of irritation when Anaflex was applied either dry and moistened or as a saturated aqueous solution (42).

Formaldehyde is slowly released by Anaflex. Haler suggested that many free oxymethylene-substituents occur within the molecule which are responsible for its strong bacteriostatic activity (41).

The effects of soil microorganisms on the degradation of urea-formaldehyde condensation products are detailed in Section XII under Biological Degradation.

IX. EFFECTS ON SOIL ORGANISMS

The effect of the soil conditioner Hygromull, (urea-formaldehyde foam in resin form which releases small quantities of formaldehyde in the soil) on plant parasitic and saprozoic nematodes was reported by De Grisse et al. (46). Sieved sandy-loam soil containing nematodes was placed in plastic bags (200 ml/bag). Hygromull (100 ml/bag) was added to ten bags and the contents were kept moist and stored at room temperature for 5 weeks. The number of plant parasitic and saprozoic nematodes in each sample was determined by washing the soil through a 250 μ sieve in a plastic basin and extracting the nematodes by the sugar-centrifugal-flotation technique. Two samples without the addition of Hygromull were processed at the start of the experiment to obtain the initial nematode population. At weekly intervals for 5 weeks, two bags with and two without Hygromull were analyzed. Results show that the population of the plant parasitic nematodes decreased linearly with time in the samples containing Hygromull (from initial population of 1430 per 100 ml soil extract to 90 per 100 ml after 4 weeks of treatment) and remained at the low level at the end of 5 weeks. Control populations fluctuated between 1100 and 1560. The population of the saprozoic nematodes decreased during the first two weeks of treatment and reached the lowest count after 3 weeks (280 per 100 ml soil extract, from an initial count of 980), then started to increase again reaching 775/100 ml soil extract after 5 weeks of treatment. Control counts varied from 760 to 1130/100 ml soil extract (46).

Huengens also used Hygromull mixed with pine litter (containing 0, 33, 50, 67 or 100% Hygromull) in azalea cultures to study its effect on soil fuana (47). Organisms counted were lumbricidae, enchytracidae, and sciaridae. After 6 months fewer lumbricids, enchytracids, and sciarids were found in mixtures containing 50% or more Hygromull. The author concluded that in these experiments it could not be proven whether the smaller number of organisms counted was the result of the release of formaldehyde by the urea-formaldehyde resin, or the lack of food supply in the Hygromull-rich mixture.

X. EFFECTS ON PLANTS

Completely polymerized urea-formaldehyde resins are not toxic in plants and cannot be broken down to supply nitrogen for plant growth (61). The low and intermediate molecular weight condensation products have been used as fertilizers to provide nitrogen at a steady rate for a prolonged period of time, but are not suitable as a quick fertilizer to supply readily available soluble nitrogen. Various plants, such as tomatoes and Sudan grass (48), corn (49), oats and millet (50), pine seedlings (51), azalea (47) and turf-grass (52,53), have been used to test the effect of low and intermediate molecular weight condensation products as fertilizers, but no adverse effects in plants have been reported (see section on Biological Degradation).

The gaseous products from incineration of urea-formaldehyde resins (formulation not reported) are highly toxic. One-week-old seedlings (summer squash, alfalfa, mustard, blue grass, and northern green bean) were killed in 10 minutes when exposed to the combustion effluent; two-week-old plants were stunted and bleached but not killed. The effluent was produced by heating 25 g of urea-formaldehyde resin in the hot zone of an incinerator (about 1100°C). Before passing into the exposure chamber, the effluent was kept above the dew point to prevent condensation and adjusted to 24°C and 50% humidity with cool dry air. Analysis of the effluent revealed carbon dioxide, carbon monoxide, methane and large quantities of ammonia and hydrogen cyanide (10, see Chemical Degradation, section XII).

25

XI. PHARMACOKINETICS

The nitrogen in urea-formaldehyde resin did not seem to be metabolized
and subsequently made available when used as animal feed for lambs. Re-
placing increasing quantities of urea nitrogen in the lambs' feed by Uramite,
a commercial preparation of urea-formaldehyde resin, resulted in increased
non-protein nitrogen excretion (39).

There is no other information available on absorption, distribution,
and metabolism of urea-formaldehyde resins.

XII.   OCCURRENCE, DISPERSION AND FATE IN THE ENVIRONMENT

In this section the occurrence, persistence, transport and dispersion, chemical and biological degradation and bioaccumulation of urea-formaldehyde resins in the environment will be discussed.

A.   OCCURRENCE

Urea-formaldehyde resins are synthetic products and do not occur in nature. They are widely used in moldings, buttons, screw caps, electrical insulators, plugs, sockets, and eating utensils, as adhesives in laminated boards, chipboards, and furniture manufacture; as surface coating enamels for cars, refrigerators, washing machines and stoves; in construction work to solidify loose soil and prevent seepage of underground water; and as thermal insulators (applied as foams to fill wall cavities). The low molecular weight condensation products are particularly used in treating textiles to produce water repellent and wrinkle resistant fabrics, and in manufacturing wet-strength paper. Depending on the molar ratio of urea to formaldehyde, different resins can also be used as antibacterial drugs in fertilizers. Thus, people in the modern world are in daily contact with urea-formaldehyde resins.

B.   PERSISTENCE

The completely polymerized urea-formaldehyde resins are chemically and physiologically inert in ambient conditions and thus will persist in the environment. They do not ignite but will burn in a flame giving off various gaseous products depending on the combustion temperature (see Chemical Degradation). The partially polymerized, low molecular weight condensation products, however, can degrade gradually with time and release formaldehyde vapor. When used as fertilizer, they are broken down by soil microflora to simple nitrogenous compounds (48-55, 60-63). (See section on Biological Degradation).

C.   DISPERSION

No studies on the dispersion of urea-formaldehyde resins per se are available in the literature. The completely cured urea-formaldehyde resins are presumably dispersed as solids in the finished products or as powder and dust in manufacturing plants. The incompletely polymerized low molecular weight products can be found in the leaching water soon after they are applied as fertilizer but before they are broken down by soil microflora (51, 54,55). In such manner, they can be dispersed in streams and rivers.

27

D. DEGRADATION

Under ordinary use-related conditions, the completely polymerized urea-formaldehyde resins are very stable. However, they decompose in boiling water and in hot concentrated acids and alkalis, releasing formaldehyde and ammonia. Completely polymerized resins are not digested and metabolized by animals, but the low molecular weight condensation products are degraded by soil micro-organisms. In the following sections, the chemical and biological degradation of these resins are discussed.

1. CHEMICAL

Although urea-formaldehyde resins are chemically inert under ordinary use-related conditions, they are decomposed in hot concentrated alkalis with the evolution of ammonia, and in hot concentrated acids giving off formaldehyde and formic acid fumes (4). They also undergo thermal decomposition releasing formaldehyde and other gaseous compounds (carbon dioxide, carbon monoxide, hydrogen cyanide etc.) at higher temperatures (9-12). When chipboard is exposed to 100% relative humidity at 38°C it releases formaldehyde and loses a substantial portion of its strength in 8 weeks (56).

The oxidative degradation of urea-formaldehyde resins (in butylated form) was studied by solid phase infrared spectrophotometry and gas phase vapor chromatography in the temperature region from 150° to 300°C (57). From the infrared spectra taken at 150°, 175°, 200°, 250° and 300°C, it was observed that the degradation of the resin proceeded rapidly at 200°C with the simultaneous rapid decrease of the CH_2 stretching vibration band (3.4-3.5 μ) and the C-O-C bending vibration (9.25 μ). These changes were attributed to the loss of the butoxy group. Kinetic studies on the decay of the CH_2 band gave an activation energy of 21.5 kcal which corresponds favorably with the values obtained for the oxidation of phenolic resins. The decay of the vibration bands of hydroxyl, amino and carbonyl groups proceeded at a slower rate. Above 250°C all bands disappeared rapidly as a result of the volatilization of the entire polymer. From vapor phase chromatographic studies, roughly equimolar quantities of carbon dioxide and butanol were detected at degradation temperatures from 150° to 200°C. Above 250°C, small amounts of butene, butyric acid, paraformaldehyde and water could be detected.

From these results, the oxidative degradation reactions of urea-formaldehyde were postulated as follows:

28
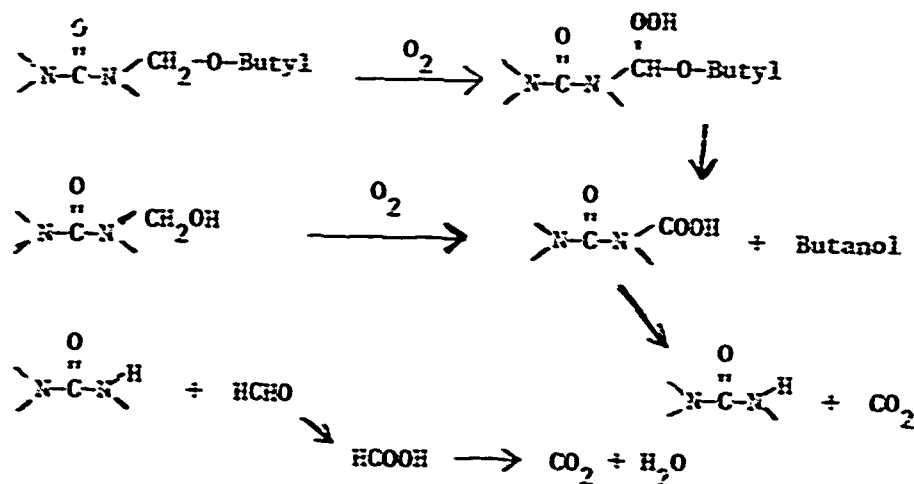
The toxic effects of the gaseous products released by incineration of urea-formaldehyde resins on rats and plants have been previously reported (see Section IV. Effects on Experimental Animals and Section X. Effects on Plants). In order to determine which components in the effluent were responsible for toxicity in rats and plants, the same sample of urea-formaldehyde resin (wood flour filler) was analyzed thermogravimetrically under inefficient combustion conditions (9). A 3-step thermal degradation was observed: below 260°C there was a gradual loss of weight (14%); from 270° to 345°C a steep loss of weight occurred (57%); and from 345° to 610°C there was again a gradual loss of weight until the resin was completely combusted at 610°C. Qualitative analysis of the gaseous products by infrared spectrophotometry showed the presence of carbon dioxide, carbon monoxide, methane and large quantities of ammonia and hydrogen cyanide. Quantitative analysis of hydrogen cyanide using Orion specific ion electrodes, 100 ml/minute air flow and a 5°C/min heating rate showed 18.9 mg of cyanide per gram of sample. Carbon monoxide and hydrogen cyanide found in the combustion effluent may produce the toxic effects observed in rats since the animals recovered rapidly when removed from exposure; otherwise, death occurred.

The gaseous products from combustion of plastics, wool and pine wood were studied because many fire deaths are caused not by actual burning but by inhalation of toxic gases evolved during the fire (11). Materials containing nitrogen produce hydrogen cyanide and carbon monoxide under thermal decomposition. The concentrations of hydrogen cyanide that are fatal to humans are 270 ppm (immediately fatal), 181 ppm (10 min. exposure) and 135 ppm (30 min. exposure) (58). The effects of carbon monoxide in humans vary with duration of exposure, partial pressure of oxygen in the air, ambient temperature, work effort, carbon monoxide content of the blood, metabolic efficiency, health status, genotype and individual susceptibility (58). A concentration of 4000 ppm of carbon monoxide was reported fatal to humans in exposures of less than one hour (11).

The combustion products of urea-formaldehyde foam, wool and three other synthetic polymers containing nitrogen were analyzed by gas chromatography (11). Test samples (weighing 400-2400 mg) were introduced into a heated flask (800°C) where combustion took place. After this temperature was maintained for 2.5 minutes, the flask was cooled for 30 minutes and the gaseous products were quantitatively analyzed by gas chromatography. In order to find out whether hydrogen cyanide is a potential hazard at fires, the above procedure which favors the formation of toxic combustion products was adopted. From urea-formaldehyde foam the gaseous products were hydrogen cyanide (0.015-0.042 g/g of sample), carbon monoxide (0.032-0.077 g/g of sample) and carbon dioxide (0.34-1.35 g/g of sample). Nitrogen dioxide was not detected with any of the 5 samples.

To compare the toxicity of a combustion product obtained from different materials, a toxicity index was used (11). This index is the ratio of the experimentally determined concentration of a toxic product (expressed as the volume of product when one gram of material is decomposed and the combustion products are diffused into a volume of 1 m³) to the concentration of the same product that is fatal (or dangerous) to humans in a 30-minute exposure (method of determination of the fatal concentration not given). The

toxicity index of a material which produces two or more toxic combustion products is determined by assuming that the effects are additive. The maximum toxicity indexes of the combustion products of urea-formaldehyde foam, wool and white pine were compared as follows:

| | Maximum Toxicity Index due to | | | |
	HCN	CO	CO_2	Total
urea-formaldehyde foam	0.26	0.01	< 0.01	0.27
wool	0.33	0.04	0.01	0.38
white pine	*	0.09	0.003	0.09

*not produced

   In a recent study the gaseous combustion products of ten kinds of synthetic polymers and one kind of wood (cedar) were quantitatively analyzed by infrared spectrophotometry, gas chromatography, and colorimetric tube method (12). The combustion of urea-formaldehyde (0.1 g, 800°C, air flow rate 100 1/hr) produced CO_2 (1,193 mg/g of sample) as the only detectable gaseous product. At a slower air flow rate (50 1/hr), CO (80mg/g of sample) and HCN (22 mg/g of sample) were detected in addition to CO_2 (980 mg/g of sample). At 700°C, nitrous oxide (quantity not given) was detected in the gaseous combustion products of urea-formaldehyde. Pyrolysis of the urea resins in the atmosphere of nitrogen at 700°C gave off ammonia which was detected with poor reproducibility (about 20% coefficient of variation). The total amount of nitrogen detected in the gaseous products was much less than the quantity of nitrogen present in the polymer. The authors suggested and confirmed with two synthetic polymers that some nitrogen in the polymers was converted to nitrogen gas (N_2) by the flaming combustion.

   The stability of urea-formaldehyde resins against ultraviolet degradation was studied by measuring changes in chemical structure with infrared spectra (59). A sample of the resin (Cymel 248-8, American Cyanamid Company) dissolved in n-butyl alcohol was applied as a film on the KBr plate used for infrared spectrometry. After drying under an infrared heat lamp, the sample was placed about 4 inches from the ultraviolet source (wavelength above 2000 angstroms) and irradiated in air at room temperature for 300 hours. Infrared absorption spectra were recorded before exposure to ultraviolet light and at various intervals during the irradiation period.

   No changes in physical appearance properties of the film, such as cracking, blistering or color change, were detected visually. The infrared spectral changes included a slight decrease in intensity of all bands after UV irradiation and the appearance of a new band at 4.66 µ characteristic of isocyanide and isocyanate group absorption. The intensity of this band reached its maximum after 180 hours of irradiation and remained at that level. The original 3.4 µ C-H streching band decreased 20% after the first 40 hours of exposure to ultraviolet light and remained constant upon further irradiation. It was concluded that this sample of urea-formaldehyde resin was moderately stable and the overall effect of ultraviolet irradiation upon it was small (59).

39

2. BIOLOGICAL

The highly polymerized urea-formaldehyde resins do not appear to be bio-degradable by various plants or animals. Feeding a commercial product, Uramite (containing 36.9% nitrogen), to lambs and rats up to 32% of the total nitrogen in the feed resulted in excretion of most of the Uramite nitrogen in the feces (39). The partially polymerized water insoluble condensation products, on the other hand, have been used as slow releasing nitrogen fertilizers and were found degradable by soil microflora as shown in the following reports.

Yee and Love first tried to use urea-formaldehyde condensation products as water insoluble nitrogen fertilizer in 1947 (60). Several condensation products with urea to formaldehyde molar ratios ranging from 0.88 to 2.0 were prepared and their rates of nitrification(20 mg N in 100 g of soil) were determined. Ammonium nitrate and dried blood were used as positive controls. Results showed that the condensation products with U/F ratios of 1.4-2.0 nitrified at rates approaching those of ammonium nitrate and dried blood. The most promising products for providing slowly available nitrogen sources are those with U/F ratios equal to 1.18 to 1.36 which nitrified at a constant rate for about 3 months and then at slightly reduced rates.

The involvement of soil microflora in the degradation of the urea-formaldehyde condensation products was studied by measuring the evolution of carbon dioxide, the nitrification in sterilized and unsterilized media, and the effects on plant growth in sterilized and unsterilized soils (48). Addition of the condensation products (U/F molar ratios - 1.2-1.4; 36-38% nitrogen) at rates up to 1% (20 mg nitrogen per 100 g of soil) did not in-hibit soil microbial activity but appeared to promote it. The carbon dioxide evolved was 2-3 times that produced by the addition of ammonium nitrate. Carbon in the condensation products seemed to be as available as that of soil organic matter to soil microflora. Nitrification occurred only in unsteri-lized soil as measured in the formation of nitrates during 18 weeks. The availability of nitrogenous compounds (resulting from microbial degradation of condensation products) for plant growth (Sudan grass and tomatoes) was indicated by the fact that the weights of tops and roots (6 weeks of growth) from plants grown in unsterilized soil were 2-3 times greater than that of plants grown in sterilized soil. Thus, the urea-formaldehyde condensation products are degraded by soil microflora into simple nitrogen compounds readily available for plant growth.

The effect of pH on the mineralization (decomposition into a soluble state) of the condensation products (molar ratio 0.5; 26.2% nitrogen, 59.4% of the total nitrogen being water-soluble) in 20 soils having initial pH values ranging from 3.9 to 7.8 was studied for 26 weeks (61). A sample representing higher polymerized forms of urea-formaldehyde, consisting of plastic waste milled in the laboratory, and containing 17.8% of nitrogen of which only 4.3% was water-soluble, was studied for comparison. There was an inverse correlation between the pH values of the soils and the percent of mineralization of the resins as shown in the following table:

31

| Initial | % Mineralization of the resins | | | | | |
| Soil | Low condensation products | | | Plastic wastes | | |
pH	2 weeks	8 weeks	26 weeks	2 weeks	8 weeks	26 weeks
7.8	8	29	42	3	5	10
7.0	16	45	65	3	7	21
6.0	49	81	90	14	51	76
5.0	34	70	84	12	44	59
3.9	69	78	52	45	62	69

The highest rates of nitrification for the low condensation products occurred in soils having initial pH values between 5.5-6.0. The dissolution of the products in acid soils appeared to be the result of chemical decomposition because 38% of the nitrogen in the products was rendered soluble after soaking 2 days in a solution of pH 4.0 (50% soluble in 7 days) without the action of soil microflora.

The rate of mineralization of urea-formaldehyde fertilizer has been found to follow first order reaction kinetics, and the rate increases at higher temperatures (62). Dissolution of these products has been studied by leaching analysis (51,54,55). Other crops used to study the availability of the degraded nitrogen products were corn (49), oats and millet (50), and turf grass (52,53). Since urea-formaldehyde resins are degraded slowly over a long period of time, they are most suitable for long-growing crops requiring a constant supply of available nitrogen. A long term study (7 years) on their effects on turf grass showed that although the availability of nitrogen for the first 2 years was not very efficient, at the end of the 7-year period urea-formaldehyde fertilizer gave the best results as determined by yield, color and soil nitrogen content (53).

The decomposition of four urea-formaldehyde condensation products of low molecular weights were studied in acid soil and soil neutralized with lime (63). The four products, methylene-urea, dimethylene-triurea, trimethylene-tetraurea, and tetramethylene-pentaurea, were prepared chemically under acid conditions in pure or partially purified form. Decomposition of these compounds in soil was studied by incubation in 700 g of moist soil at concentrations equivalent to 300 ppm of N expressed on the basis of oven-dry soil. Duplicate mixtures containing 0.5% calcium carbonate in soil were used to study the effect of soil pH on the decomposition of these products. The mixtures were incubated for 26 weeks at 23.5°C. The degree of mineralization of these compounds was analyzed by measuring the quantities of ammonia and nitrate formed after 1, 2, 3, 4, 8, 12, 16 and 26 weeks of incubation (63).

Results showed the rates of mineralization of these compounds decrease with increasing chain length. Methylene diurea decomposed very rapidly and completely in acid soil (pH 5.4). The addition of lime (soil pH 7.6) delayed the initiation of decomposition but still 88% of it was mineralized in 2 weeks. Dimethylene-triurea was decomposed less rapidly initially and reached completion by the end of 26 weeks in acid soil. In the presence of

lime, mineralization started after the first week and reached 82% after 26
weeks. The decomposition of trimethylene-tetraurea proceeded slowly but
steadily in acid soil and approached its maximum (81-85%) within 8 weeks.
The addition of lime delayed the initiation of decomposition but the maximum
of 67-72% was also reached in 8 weeks. The largest polymer of this series,
tetramethylene-pentaurea, decomposed very slowly in the soil and attained
only 15% mineralization in acid soil and 9% in limed soil. It was concluded
that trimethylene-tetraurea appeared to be the most promising compound as
a slow fertilizer.

E. BIOACCUMULATION

The urea-formaldehyde resins are not absorbed by plants or animals in
the polymerized form. When fed to animals the resins are excreted in the
feces (39). When applied as fertilizer in the soil, the low molecular
weight condensation products are slowly broken down by soil microorganisms
into simple nitrogenous compounds which can be utilized by plants (48-50).
Those that get into leaching water probably are degraded by soil and aquatic
microflora into simple compounds which are taken up by aquatic plants and
animals and eventually enter into the food chain (50-55). No reports on bio-
accumulation were found in the literature.

XIII. INDUSTRIAL HYGIENE STANDARDS AND PRACTICES

The safety hazards of urea-formaldehyde resins primarily involve formaldehyde which is inadvertently released into the air.

The condensation of urea and formaldehyde is an exothermic reaction. Heat generated during the reaction would increase the concentration of formaldehyde in the air causing irritation to the eyes, nose, throat and skin of exposed workers, especially individuals hypersensitive to it. In addition to the hazard during manufacturing of the resins, formaldehyde is also evolved when the condensation products are processed in molding, laminating, coating, etc., to make various end products. These products, if not completely cured, could again release small quantities of formaldehyde over a long period of time. Thus industrial safety practices center on keeping the level of formaldehyde below the threshold limit values. In the following sections the hygienic and safety practices for the manufacturing and application of urea-formaldehyde resins and the prevention of hazards due to the finished products will be reviewed.

A. THRESHOLD LIMIT VALUES (TLV) AND STANDARDS

There are no TLV or OSHA standards set for urea-formaldehyde resins in the workroom environment. The current OSHA standard for formaldehyde for 8-hour time-weighted average is 3.6 mg/m^3. The maximum ceiling limit is 12 mg/m^3 for 30 minutes duration on 8-hour shift. NIOSH recommends 1.2 mg/m^3 ceiling for 30 minutes (64).

B. INDUSTRIAL HEALTH AND SAFETY PRACTICES

Most studies of industrial hazards in the manufacture of urea-formaldehyde resins and the application of their low molecular weight products were reported outside of the United States (65-71). Within the United States, a few cases of occupational dermatoses were reported only during the early years (later thirties and early forties) when the urea-formaldehyde resins were first introduced commercially (18,19). After a completely enclosed system for the manufacture of these resins was adopted in later years, no reports of industrial hazards have been found. The safety practices thus involve engineering control and hygiene aspects as recommended by the Bureau of Industrial Hygiene, Michigan Department of Health (20).

1. ENGINEERING CONTROL ASPECTS

Operations for mixing, grinding and heating should be enclosed to prevent fumes and dust polluting the air. Adequate ventilation should be installed to remove fumes and dust in the air and frequent cleaning of dust on floor and machines by vacuum. Manual operations should be replaced by mechanical equipment to reduce direct contact with the material. The plant should be designed to place heating and drying operations in one area segregated from

the rest of the plant so that fumes will not contaminate the entire plant. Air temperature should be kept low because heat tends to intensify skin irritation (20). Industrial waste water containing formaldehyde can be treated with lime, which reduces its concentration 100-fold in 3 days (72).

2. HYGIENIC ASPECTS

Personal hygiene of workers should be emphasized. Adequate washing facilities for frequent cleaning of exposed skin and for showering at the end of the work shift, should be provided. Mild, nonirritating soap and clean towels should be available. Workers should wear protective clothing such as gloves, sleeves and coveralls, which should be laundered frequently.

Protective creams for face and other exposed parts of the body should be provided. The workers should be informed about the toxic nature of the material and instructed about the proper operative techniques. Adequate education on personal hygiene and safety measures should be given. Frequent medical check-ups should be made to detect any health problems at the early stage (20).

C. SAFETY MEASURES FOR STORAGE OF PRODUCTS

When urea-formaldehyde condensation products are used to make chipboard, to treat textiles or for thermal insulation, residual formaldehyde may be released slowly if the resin is not completely cured to form high molecular weight polymers. Thus chipboards and treated fabrics should be stored in a well-ventilated warehouse for 3 months before being shipped for the market (73,74). When urea-formaldehyde foam is used to fill wall cavities for heat insulation, the building should not be occupied for 3 months to ensure complete removal of all residual formaldehyde (68,75). Should the warehouse catch fire, it should be kept in mind that highly toxic gaseous products such as hydrogen cyanide, carbon monoxide and ammonia would be produced (9,11,12).

XIV. SAMPLING AND ANALYSIS

In this section special methods for sampling and recent methods for the
analysis of urea-formaldehyde resins and for the detection of free formalde-
hyde will be discussed.

A. SAMPLING

For detection of free formaldehyde in clothing, the entire garment is
placed in an air-tight container in which a small beaker containing a few drops
of chromotropic solution (1 g in 250 ml sulfuric acid) is placed. The quantity
of formaldehyde is estimated by measuring the time needed for the initial purple
color to appear (76).

The formaldehyde released in the air from chipboards is estimated by the
intake of 50 liters of room air through a washing bottle and analyzing the
extract by the general procedure (74), or by the air being pulled through a
solution containing the chromotropic reagent (77).

B. ANALYSIS OF UREA-FORMALDEHYDE RESINS

Completely polymerized resins, as well as their low molecular weight
condensation products, can be analzyed by paper chromatography, thin-layer
chromatography, gas chromatography, gel-permeation chromatography, infrared
spectrophotometry, polarography and proton magnetic resonance methods. These
will be discussed as follows:

1. PAPER CHROMATOGRAPHY

The aminoplasts in glues, hardened glue joints, varnishes and impregnated
paper can be detected and separated by paper chromatography (78). The ground
sample (1-2 g) is hydrolyzed in hydrochloric acid (25%, density 1.25) and a
few drops of hydrogen peroxide for 15 minutes. After spotting on Schleicher
and Schüll 2043b paper, it is developed with butanol:acetic acid:water (4:1:5)
and dried at 35°C. The paper is sprayed with 0.5% dimethylaminobenzaldehyde
in isobutyl alcohol and treated with hydrochloric acid vapor. Bright lemon
yellow spots for urea (Rf 0.41-0.43) appear after 2-6 minutes; for melamine,
the spots are corn yellow (Rf 0.22-0.24) and appear after 7-12 minutes.

2. THIN-LAYER CHROMATOGRAPHY

Urea-formaldehyde condensation products of low molecular weight (less
than 200) can be qualitatively detected by thin-layer chromatography (79).
The plates (Merck Kieselgel F$_{254}$, fast running) are pre-treated with ammonia
vapor immediately before sample application to prevent further condensation
during chromatography. The condensation mixture is applied as a 20% solution
in methanol-water (1:1) and developed with: (1) ethyl acetate:methanol:ammonium
hydroxide, Sp. gr. 0.880, (80:6:6) for separation and detection of ethers and
methylol compounds of urea; (2) ethyl acetate:methanol:ammonium hydroxide,
Sp. gr. 0.880, (80:15:5) for separating mixtures of methylenediurea, methylol
methylene diurea and dimethylenetriurea.

36

The developed plates are dried at room temperature for 15 minutes, and exposed to chlorine gas for a few seconds. After allowing the excess chlorine to disperse, the plates are sprayed with 5% o-toluidine in glacial acetic acid. Full color develops in 8 hours (plates kept in dark) and is stable for several weeks. Urea and methylenediurea appear as blue spots; formaldehyde, dimethylol urea, etc., as yellow spots; and monomethylol urea, etc., as green spots. The Rf values are given in a graph.

Quantitative estimation of these low molecular weight condensation products is accomplished by converting these compounds to their methyl ethers with methanolic boron trifluoride. These ethers are stable and easily separable from each other and from high molecular weight condensates on thin-layer chromatography (80). The procedure consists of adding 0.5% boron trifluoride (in methanol) dropwise with vigorous stirring to 1 g (or less) of sample to a final volume of 5 ml. The thin-layer plate (Merck Kiesegel F_{254}) is pretreated with the vapor of the developing solution (ethyl acetate:methanol: ammonium hydroxide, Sp. gr. 0.880, 44:3:3) before application of the sample. After development, the plate is treated with chlorine gas and sprayed with 5% o-toluidine solution as described previously. Urea appears as blue spots after 30 minutes, monomethylolurea monomethyl ether as green spots, and dimethylolurea dimethyl ether as yellow spots. (Rf values are not given, but the position of spots is shown in a chromatogram.)

3. INFRARED SPECTROPHOTOMETRY

The amount of urea-formaldehyde resin (0.3-3.0%) in wet-strength paper can be measured by differential infrared spectrophotometry (81). The paper samples are made translucent with an immersion oil whose refractive index is close to that of the paper, and the samples are analyzed directly by placing them between sodium chloride plates. Any material commonly found in the paper that might interfere with spectral analysis is removed by exhaustive Soxhlet extraction with carbon tetrachloride and methylethylketone. A standard paper is chosen for the reference beam. Commercial resin samples were analyzed by casting the resin on sodium chloride plates and obtaining the spectra before and after curing the sample at 105°C for 1 hour. The aliphatic C-H stretching band at 3.4 μ is used as an internal standard.

4. POLAROGRAPHIC METHOD

Colloids, high molecular weight substances and dyes will decrease the polarographic maxima of oxygen. This suppression is used as a criterion for the evaluation of sanitary safety of plastics, such as polyvinyl alcohols, polyamides, polyvinyl butyrals and urea-formaldehyde resins (82). The samples (2.5 g or 100 cm^2) were extracted with 100 ml of water for 10 days. Plastics that show less than 50% suppression of the oxygen maxima of the polarographic curve are regarded as sanitarily acceptable.

5.   COMBINATION METHOD

Recently a combination method for the analysis of low molecular weight condensation products of urea-formaldehyde by the application of gas chromatography, mass spectrometry, gel-pe. eation chromatography and proton magnetic-resonance was reported (83). These condensation products ar converted into volatile derivatives for gas chromatographic analysis by sil ation with N,O-bistrimethylsilyl-trifluoro-acetamide (BSTFA) in dimethyl formamide. The gas chromatogram was analyzed by mass spectrometry to obtain the exact amounts of urea, monomethylolurea and dimethylolurea in the resin. Gel permeation chromatography is used to separate low molecular weight mixtures (by using Sephadex LH20, 50-60 μ, in water) and high molecular weight products (by using Styragel, 3 x 10^4 Å and 3 x 10^5 Å, in dimethyl formamide). Proton magnetic resonance spectra are used to analyze the presence of functional groups in urea-formaldehyde resins (83,84).

C.   ANALYSIS OF FREE FORMALDEHYDE

Although formaldehyde is not the main topic for this study, methods of analysis for it will be discussed briefly because it is the major cause of health hazards of urea-formaldehyde resins. The most commonly used reagent for free formaldehyde is chromotropic acid. Other reagents are Schiff's reagent, "Purpald," and acetylacetone plus ammonium salts.

1.   CHROMOTROPIC ACID METHOD

Formaldehyde reacts with chromotropic acid (1,8-dihydroxynaphthalene-3,6-disulfonic acid) in the presence of sulfuric acid to give an intense purple color which can be quantitatively estimated at 570-580 nm. This reagent is specific for formaldehyde and will not react with other aldehydes which give positive reactions with the classical Schiff's reagent. For high concentrations of formaldehyde, the purple color appears within minutes; but more than 10 hours for low concentrations of formaldehyde. The development of color can be speeded up by heating the solution at 100°C for 30 minutes. Variations of this method have been employed to detect free formaldehyde in fabric samples, in clothing, in chipboard, in plastic utensils and in the air (74,76,77).

The general procedure consists of reacting 5 ml of a water extract of the sample with 1 ml of 5% chromotropic acid and 5 ml of concentrated sulfuric acid. After heating at 100°C for 30 minutes the color developed is measured at 570 nm spectrophotometrically (15,85,86).

2.   OTHER REAGENTS

The classical aldehyde reagent, Schiff's reagent, can be used to detect formaldehyde, but the results are not specific because other aldehydes also react with this reagent.

Trace amounts of formaldehyde react with a reagent containing acetyl-acetone and an excess of ammonium salt to give a yellow product (diacetyld i-hydrolutidine) which can be measured at 412 nm. The product is also strongly fluorescent under soft ultraviolet light. The conditions for this reaction are mild enough to permit its use with living materials (87).

"Purpald" (4-amino-3-hydrazino-5-mercapto-1,2,4-triazole) is a new reagent that reacts with formaldehyde to give a purple color (λ max = 550 nm) in 1 N sodium hydroxide solution (88). This reaction is so sensitive that the limit of detection is 5 ng of formaldehyde per ml (0.005 ppm) which is below the limit of odor detectability (0.88 ppm) and maximum permissible industrial level (6 mg/m^3 of air). Therefore, this reagent has been used to check air quality of factories and to assess the efficiency of curing in chipboard. For the latter, spot tests on chipboard with one drop of 1% purpald in 1 N sodium hydroxide give a purple color when the resin is not completely cured and formaldehyde is present (88).

TECHNICAL SUMMARY

Urea-formaldehyde resins are a mixture of condensation products of urea and formaldehyde. The composition and structure of these products depend on the a) molar ratio of the two components, b) conditions of the reaction (pH, temperature, catalyst, etc.) and c) degree of polymerization and cross-linkage. These resins are thermosetting plastics used extensively in adhesives, molding, lamination, coating, insulation and textile and paper treatment. The subjects covered in this report include physical and chemical properties, toxicity in humans and animals, effects on plants, microorganisms and soil organisms, pharmacokinetics, fate in the environment, industrial hygiene and safety practices, sampling and analysis.

A. PHYSICAL AND CHEMICAL PROPERTIES

The properties of urea-formaldehyde resins depend greatly upon the degree of polymerization of the product. Low molecular weight products exist either as a viscous liquid (neutral or alkaline pH) or a white powdery solid (acid pH). They are converted by heat (heat-cured) or acid (acid-cured) into high polymeric forms which are water-insoluble, amorphous solids (1-3).

The simple condensation products ("monomers and dimers") are viscous liquids which are soluble in water and alcohol and decompose easily with the release of formaldehyde. Intermediate products are amorphous powders which are soluble in pyridine, aqueous formaldehyde, formic acid and dilute mineral acids. They are gradually decomposed in acid medium under ambient conditions slowly giving off formaldehyde (1-4).

The cured, high, molecular weight final products are colorless, transparent, odorless and tasteless solids. They are insoluble in cold water and cold dilute acids and alkalis but decompose in boiling water and hot strong acids and alkalis. They are unaffected by common organic solvents, oil and grease (1-3). Various fillers, such as cellulose and wood flour, are added to the resins to improve their strength and quality. Alcohol derivatives are introduced to increase their solubility in non-aqueous solvents (1-3). Although these resins do not catch fire on free flame, they do decompose upon pyrolysis giving off gaseous products such as carbon monoxide, hydrogen cyanide, carbon dioxide and ammonia (9-12).

Since there is no single formula for urea-formaldehyde resins, it should be kept in mind that the products used for investigations discussed in this report vary in their composition and the quantities of free formaldehyde present in the resins. The presence of free formaldehyde influences greatly the effects of the resins on humans, animals, plants, microorganisms and the environment.

B. HUMAN TOXICITY

In view of the literature available to date, the completely cured urea-formaldehyde resins do not appear to be toxic. Toxic effects could arise from

the highly polymeric forms of resins during pyrolysis where toxic gaseous products, such as hydrogen cyanide, carbon monoxide, and ammonia, are generated -12).

Most of the reported adverse reactions pertaining to urea-formaldehyde -ins are mainly due to formaldehyde which is produced by:

a. incompletely reacted starting material,

b. slow decomposition of low molecular weight condensation products,

c. decomposition of the resin by heat which is generated during industrial processing such as molding, laminating, high speed sawing, etc.,

d. slow release from resin treated fabric, paper and chipboard.

Formaldehyde is well known to be highly irritating to eyes, skin and mucous membrane. Since a detailed report on the toxicity of formaldehyde appeared in a NIOSH criteria document (13), only a brief discussion on the various effects of formaldehyde produced f·om the incompletely cured resins are reported here.

1. Eye Exposure

Fabrics that are improperly treated with urea-formaldehyde resins and insufficiently washed before marketing would release formaldehyde slowly into the air. Stores selling such fabrics were found filled with formaldehyde fumes which caused excessive lacrimation in shopkeepers and customers (14,15)

2. Inhalation

Formaldenyde was detected in the blood of workers who had been exposed to urea-formaldehyde resins. The blood formaldehyde levels were highest soon after work and disappeared 18 hours later (16). Female workers exposed to various concentrations of formaldehyde suffer menstrual disorders and complications during pregnancy; children born were underweight (17).

3. Skin Contact

Formaldehyde released from urea-formaldehyde resins may cause dermatoses to persons exposed to it. People may come into skin contact with formaldehyde occupationally or through using products which have been improperly treated with urea-formaldehyde resins. Most of these cases were reported outside of the United States.

a. Occupational Dermatoses

Workers engaged in manufacturing, molding, laminating, applying adhesives, etc. are exposed to formaldehyde released during the process. Dermatoses

41

usually develop on the hands and forearms of these workers (16-29).

b. Contact Dermatoses due to Use of Treated Products

People wearing clothing made of fabrics that was improperly treated with urea-formaldehyde resins may develop dermatoses around the neck and waist and under arm area (15,30-36).

C. EFFECTS ON ANIMALS

Completely cured urea-formaldehyde resins are not considered to be toxic, and there are only a few reports which describe effects of these resins on animals.

The acute oral toxicity of urea-formaldehyde resins was determined in 6 groups of guinea pigs (5 per group) by oral administration (inserted down the esophagus) of single doses of 480-2320 mg/kg body weight. No animals died during the test or through the observation period of 8 days. No pathological changes were observed (37).

The subchronic oral toxicity of the resin was determined in rats (strain, sex, age and number not given) by giving daily doses of 1 g/kg body weight in the form of a 20% polysorbate solution administered with a pharyngeal tube for 9 weeks. No histological abnormalities were found in the liver, kidney or intestinal tract of the rats (37).

Lambs fed diets containing 2, 4, 8, 16 or 32% of the resin replacing equivalent quantities of urea (control diet contains 100% urea) for 10 days showed no toxic effects. Much of the nitrogen in the resin was excreted in the feces (39).

When two urea-formaldehyde resins containing different quantities of free formaldehyde (one contained 29%, the other 1.2%) were applied on the skin of 10 albino guinea pigs. 7 out of 10 and 8 out of 10 animals, respectively, developed erythema and other skin irritations. It was concluded that the sensitizing effect was not due to free formaldehyde (23).

D. CARCINOGENICITY, MUTAGENICITY AND TERATOGENICITY

No reports on carcinogenicity, mutagenicity and teratogenicity of urea-formaldehyde resins were found in the literature.

E. EFFECTS ON DOMESTIC ANIMALS AND WILDLIFE

No reports on the effects of urea-formaldehyde resins on wildlife were found in the literature. In the only report available on domestic animals, lambs were fed diets containing 2-32% of the resins for 10 days without effects (39) (see Effects on Animals).

F. EFFECTS ON AQUATIC ORGANISMS

No studies on the effects of urea-formaldehyde resins on aquatic organisms were found in the literature.

G. EFFECTS ON MICROORGANISMS

The completely cured urea-formaldehyde resins in highly polymerized forms have no apparent effects on microorganisms (40).

The low molecular weight condensation products with urea to formaldehyde ratio greater than unity (U/F > 1) have been used as fertilizers because soil microorganisms can attack and degrade these products to provide soluble nitrogen for growing plants (see Biological Degradation in Section XII).

When the urea to formaldehyde ratio is less than unity (U/F < 1), the low molecular weight condensation products such as Anaflex exhibited an antibacterial action which has been applied clinically to treat certain skin infections. A total of 37 species (580 strains) of bacteria and fungi were tested. All, except 6 strains, were found sensitive to the resin; viruses of herpes simplex, vaccinia and poliomyelitis were not affected (37,41,42). Clinical tests on more than 200 patients representing 238 cases of various skin infections showed that 80% of those with furunculosis were cured within 4 days (41-43).

It has been assumed that the antibacterial action of Anaflex was due to free formaldehyde in the product. However, chemical analysis with aldehyde reagent and skin tests with a single rabbit and a human volunteer, which were both hypersensitive to formaldehyde showed that the sample of Anaflex did not contain free formaldehyde. Thus the resin itself may exert an antibacterial action (41,42). This is contrary to the results found by other investigators.

H. EFFECTS ON SOIL ORGANISMS

When an urea-formaldehyde foam used as soil conditioner was added to the soil at 100 ml per 200 ml soil extract, the population of parasitic nematodes decreased linearly with time and stayed at the low level for 5 weeks. The population of saprozoic nematodes decreased during the first 2 weeks of treatment, reached the lowest level after 3 weeks, and started to increase again thereafter (46).

The same soil conditioner preparation (0,33,50,67, and 100% Hygromull) was mixed with pine litter in azalea cultures. After 6 months, the population of lumbricids, enchytracids, and 4 species of mites was reduced in mixtures containing higher percentages of the resin (47).

I. EFFECTS ON PLANTS

The completely polymerized urea-formaldehyde resins have not been reported to be toxic to plants. Since they are chemically inert at ambient conditions,

43

they are not likely to be broken down by soil microorganisms to supply nitrogen
for plants under neutral conditions, but may be slowly degraded in acid pHs.
The low and intermediate molecular weight condensation products have been used as
fertilizers which release nitrogen slowly at a steady rate over a long period
of time. These are not suitable as quick fertilizers that supply readily
available nitrogen (see Biological Degradation in Section XII)).

No adverse effects on plants have been reported when these products were
used as fertilizers for tomatoes and Sudan grass (48), corn (49), oats and
millets (50), pine seedlings (51), azalea (47) and turf grass (52,53).

The gaseous products obtained from pyrolysis of urea-formaldehyde resins
are highly toxic. One-week-old seedlings of summer squash, alfalfa, mustard,
blue grass and northern green beans were killed in 10 minutes when exposed
to the combustion effluent; two-week-old plants were stunted and bleached but
not killed (10, see Chemical Degradation in Section XII).

J. PHARMACOKINETICS

No detailed reports on the absorption, distribution, metabolism and ex-
cretion of urea-formaldehyde resins were found in the literature. The nitrogen
in urea-formaldehyde resin did not seem to be metabolized and was excreted
in the feces by lambs which were fed a diet containing the resin as a supple-
mental nitrogen source (29).

K. OCCURRENCE, DISPERSION AND FATE IN THE ENVIRONMENT

1. Occurrence

Urea-formaldehyde resins are synthetic products; they do not occur in
nature. Cured resins are widely used in molding, laminating, surface coating,
insulation, as adhesives and in treatment of textiles and paper. In addition,
the low molecular weight condensation products can also be used as an anti-
bacterial agent or a fertilizer depending on the molar ratio of urea and
formaldehyde (see Section VIII and XII).

2. Persistence

The completely polymerized urea-formaldehyde resins are chemically and
physiologically inert under ambient conditions and thus will persevere in the
environment. Upon pyrolysis, they break down into various gaseous compounds
depending on the combustion temperature (see Chemical Degradation in Section
XII). The low molecular weight condensation products decompose gradually giving

off formaldehyde and other simple nitrogenous compounds by soil microflora
(see Biological Degradation in Section XII).

3. Transport and Dispersion

No studies on the dispersion of urea-formaldehyde resins were found in
the literature. The completely polymerized resins presumably are trans-
ported and dispersed as solids. Some of the low molecular weight condensa-
tion products are soluble and can be found in leaching water when they are
used as fertilizers (51,54,55).

4. Degradation

a. Chemical

Although the completely polymerized resins are chemically inert under
ordinary use-related conditions, they are decomposed in hot concentrated alkali,
releasing ammonia, and in hot concentrated acids, giving off formaldehyde
and formic acid fumes (4).

Under oxidative thermal decomposition, the butylated resin produced
carbon dioxide and butanol at temperature range 150-200°C. Above 250°C,
small amounts of butene, butyric acid, paraformaldehyde and water were de-
tected (57).

A sample of urea-formaldehyde resin with wood flour filler was analyzed
thermogravimetrically under inefficient combustion conditions and revealed a
3-step degradation: a gradual loss of weight below 260°C, a steep loss of
weight from 270° to 345°C, and again a gradual loss of weight until the resin
was completely combusted at 610°C (9). Qualitative analysis showed the
presence of carbon dioxide, carbon monoxide, methane and large quantities of
ammonia and hydrogen cyanide (9).

A comparison of the combustion products of urea-formaldehyde resins,
wool and white pine showed that combustion of wool produced more hydrogen
cyanide and carbon monoxide than the resin. No hydrogen cyanide was produced
from combustion of white pine (11).

The rate of air flow and temperature influence the combustion products
of the resin. At 800°C and 100 l/hr air flow rate, only carbon dioxide was
detected. At a slower air flow rate (50 l/hr), carbon monoxide and hydrogen
cyanide also appeared. At 700°C, nitrous oxide was detected. Pyrolysis
of the resin in an atmosphere of nitrogen at 700°C released ammonia (12).

The stability of urea-formaldehyde resins against ultraviolet irradiation
was studied by applying a film of the resin on the KBr plate of the infrared
spectrophotometer. After ultraviolet irradiation for 300 hours, no changes
in physical appearance of the film were observed. Infrared spectrometry
studies showed only a slight decrease in intensity of all the bands and the
appearance of a new band characteristic of isocyanide and isocyanate group
absorption (59).

b. Biological

The highly polymerized urea-formaldehyde resins do not appear to be metabolized and degraded by plants and animals. Under slightly acidic conditions (pH 5-6), the completely cured resins may be partly degraded by soil microflora over a long period of time (26 weeks) (61).

The low molecular weight condensation products are degraded by soil microflora to provide soluble nitrogen sources for plant growth. The most promising products for use as fertilizers were found to have U/F molar ratios equal to 1.2-1.4 (48.60). Involvement of microflora for the degradation of the resin was confirmed by measuring the evolution of carbon dioxide, the extent of nitrification and effects on plant growth in sterilized and unsterilized soil (48).

The effect of pH on the mineralization of the condensation products was studied for 26 weeks in 20 soils having initial pH values ranging from 3.9 to 7.8 (61). The highest rates of nitrification occurred in soils with pH values of 5.5-6.0. Soil microflora did not seem to play a role in acid degradation.

The rate of mineralization of urea-formaldehyde fertilizer was found to increase with higher temperatures following first order reaction kinetics (62).

A long term study (7 years) with turf grass showed that urea-formaldehyde fertilizer gave the best results at the end of the study as determined by yield, color, and soil nitrogen content (53).

The decomposition in soil of 4 simple condensation products of urea and formaldehyde with known chemical structures showed that the rate of mineralization decreased with increasing chain length (63). Methylene diurea decomposed very rapidly and completely in acid soil (pH 5.4). Dimethylene-triurea degraded less rapidly and reached completion by the end of 26 weeks in acid soil. The decomposition of trimethylene-tetraurea proceeded slowly and steadily in acid soil and appeared to be most promising as a slow fertilizer. Tetramethylene-pentaurea decomposed very slowly and reached only 15% mineralization at the end of 26 weeks. The addition of lime to the soils reduced the rate of mineralization of all the compounds tested.

5. Bioaccumulation

No reports on bioaccumulation of urea-formaldehyde resins in the environment were found in the literature.

L. INDUSTRIAL HYGIENE STANDARDS AND PRACTICES

Since the highly polymerized urea-formaldehyde resins and urea itself are not considered to be toxic, the industrial hazards involve mainly the formaldehyde which is inadvertently released into the air.

1. Threshold Limit Values (TLV) and Standards

There are no TLV or OSHA standards set for urea-formaldehyde resins in the workroom environment. The current OSHA standard for formaldehyde for 8-hour time-weighted average is 3.6 mg/m^3. The maximum ceiling limit is 12 mg/m^3 for 30 minutes during an 8-hour shift. NIOSH recommends 1.2 mg/m^3 ceiling for 30 minutes (64).

2. Industrial Health and Safety Practices

Most of the industrial hazards in the manufacture and application of these resins were reported outside of the United States (67-71). A few cases of occupational dermatoses were reported in the United States only during the early years of commercial application of these resins (18,19). After a completely enclosed system for their manufacture was adopted, no reports of industrial hazards have been found. The safety practices involve engineering and medical aspects as recommended by the Bureau of Industrial Hygiene, Michigan Department of Health (20).

a. Engineering Control Aspect

The recommended safety practices are: enclosed operation, adequate ventilation, cool room temperature, mechanical operation, and segregated operations in the plant. Waste water containing formaldehyde can be treated with lime to reduce its concentration 100-fold in 3 days (72).

b. Hygiene Aspects

Personal hygiene of workers is important. Frequent washing of exposed skin, protective clothing and creams, and adequate education of workers and medical check-ups are recommended (20).

3. Safety Measures for Storage of Resins

The slow release of formaldehyde from incompletely cured resin should be considered during storage. Fire hazards that might generate toxic gases such as hydrogen cyanide, carbon monoxide and ammonia from the resin should be prevented.

M. ANALYSIS

The methods used for the analysis of urea-formaldehyde resins include paper chromatography, thin-layer chromatography, and infrared spectrophotometry (78,80,83,84). Free formaldehyde can be analyzed by chemical methods which include reaction with chromotropic acid, Schiff's reagent, or Purpald (15,85-88).

ENVIRONMENTAL IMPACT

From the available literature it is clear that urea-formaldehyde resins differ greatly in their composition, degree of polymerization, and content of free formaldehyde. The toxicity of the resins on humans and animals and the effects on plants, microorganisms and soil organisms also vary according to the quantity of free formaldehyde present in the sample. In general, the effects of these resins on the environment can best be discussed according to their degree of polymerization.

The highly polymerized resins are very stable under ordinary conditions. Since they are not degraded by soil microflora to any appreciable extent, it is likely that they probably will persist in the environment even though bio-accumulation studies have not been conducted. This type of resin is only broken down by incineration when various gaseous products, such as hydrogen cyanide, carbon monoxide, carbon dioxide, ammonia, etc., are released depending on combustion conditions.

The low molecular weight condensation products are very unstable and do not tend to accumulate in the environment. They are easily decomposed especially under hot humid weather to release free formaldehyde. Their effects on microorganisms depend on the proportion of urea and formaldehyde in tre product. When the quantity of urea is less than that of formaldehyde, the product has antibacterial activity due to the slow release of formaldehyde, and has been applied clinically to treat certain skin infections. When excess urea is present in the product, no harmful effects on microorganisms have been observed. On the contrary, the product has been used as fertilizer which is degraded by soil microflora to produce soluble nitrogen compounds for growing plants. Thus, the highly polymerized resins are not degraded and tend to accumulate in the environment, whereas the low molecular weight condensation products are degraded to release formaldehyde and other nitrogenous compounds. If the product is not confined in a limited space, the released formaldehyde could be dissipated in open air and washed down and diluted by rainwater. The nitrogenous breakdown compounds, if not completely taken up by plants, will be carried by leaching water to streams where they may be absorbed by aquatic organisms and plants and eventually enter into the food chain; however, reports as to the effects of these resins on aquatic organisms, birds, and wildlife are not available in the literature.

RECOMMENDATIONS FOR FURTHER STUDIES

Urea-formaldehyde resins can be regarded as two types of polymers: the highly polymerized products that are stable and not considered to be toxic, and the low molecular weight condensation products that decompose easily to release formaldehyde. The properties and effects of each are quite different. Resins produced from different sources contain various quantities of free formaldehyde, e.g., MF-17, 29% formaldehyde, UKS, 1.2%. This variation should be considered when evaluating studies performed by different investigators. Thus, carefully controlled toxicological studies with chemically analyzed resin samples should be conducted.

The following gaps in toxicological and environmental data are listed in Table IV for both types of resins. The important points are:

1. To ascertain the degree of polymerization and the amount of free formaldehyde in the resin to be tested, because the content of formaldehyde affects the toxicity of the resins.

2. To initiate Phase I toxicological studies (see Table IV). Although inhalation and dermal studies have been undertaken by Russian investigators, detailed experimental conditions and controls were not reported clearly in their studies, which makes them of limited utility. These investigations were not considered in preparing Table IV.

3. To consider initiation of Phase II and Phase III studies. Studies assaying reproductive and teratogenic effects, carcinogenicity or other chronic diseases are unavailable.

49

TABLE IV

GAPS IN TOXICOLOGICAL AND ENVIRONMENTAL DATA
ON UREA-FORMALDEHYDE RESINS

Phase I:	
Acute oral LD_{50}	X
Acute inhalation LC_{50}	X
Eye irritation	X
Skin sensitization	X
Metabolism[a]	X
Mutagenesis	X
Phase II:	
Subacute inhalation studies	X
Phase III:	
Chronic inhalation studies	X
Fertility, reproduction	X
Teratology	X
Metabolism[b]	X
Environmental Studies:	
Effects on aquatic organisms	X
Effects on plants[c]	
Effects on domestic animals	X
Effects on wildlife	X
Biodegradation	

[a] Metabolism will include absorption, distribution, excretion, and pharmaco-kinetics, using radio-labeled material.

[b] This will include the identification and possible isolation of any metabolities.

[c] Tests should be run if the specific plant receiving the resin has not been so tested.

X marks indicate that an adequate study has not been undertaken.

BIBLIOGRAPHY

1. Widmer, G.: Amino resins. Encyclopedia of Polymer Science and technology. Interscience Publisher, New York, 1964, 2:1-94.

2. Wohnsiedler, H. P.: Amino resins and plastics. Kirk-Othmer, Encyclopedia of Chemical Technology; John Wiley and Sons, New York, 1963 (Second Edition), Vol. 2, pp. 225-258.

3. Mills, D. C., J. H. Briston: Aminoplasts. Polymer Technology; Chemical Publishing Company, Inc., New York, 1965, pp. 52-62.

4. Di Palma, S.: [Compound obtained by treating urea with formaldehyde.] Boll Chim Farm 51:78-79, 1912 (Italian).

5. Barsky, G.: Urea-formaldehyde and related resins. Colloid chemistry, theoretical and applied, by selected international contributors, J. Alexander – ed., Reinhold Publishing Corp., New York, 1946, Vol. VI, pp. 1035-1038.

6. Anonymous: Amino resins. The Plastics Manual, The Scientific Press Ltd., London, 1971 (Fifth Edition), pp. 14-17.

7. Roff, W. J., J. R. Scott, J. Pacitti: Handbook of common polymers, fibres, films, plastics and rubbers. Chemical Rubber Company Press, Cleveland, Ohio, 1971, Sec. 27:285-298.

8. Rodgers, Jr., J. L.: Melamine molding compounds. Plastics Resins Ind 2(6):17, 21-23, 1943.

9. Boettner, E. A., G. L. Ball, B. Weiss: Combustion products from the incineration of plastics. NTIS Publ No 222-001, 1973.

10. Heimburg, R. W.: Environmental effects of the incineration of plastics. AIChE Symp Ser 68(122):21-27, 1972.

11. Sumi, K., Y. Tsuchiya: Combustion products of polymeric materials containing nitrogen in their chemical structure. J Fire Flammability 4(1):15-22, 1973.

12. Morimoto, T., K. Takeyama, F. Konishi: Composition of gaseous combustion products of polymers. J Appl Polym Sci 20(7):1967-1976, 1976.

13. Anonymous: Criteria for a recommended standard...occupational exposure to formaldehyde. HEW Publ. No. (NIOSH) 77-126, U.S. Department of Health, Education, and Welfare, Washington, D.C., 1976.

14. Tojo, H., M. Tsuji: [Lacrimal effect of synthetic fibers]. Nippon Ganka Kiyo 16:321-322, 1965 (Japanese).

15. Hovding, G.: Contact eczema due to formaldehyde in resin finished textiles. Acta Derm Venereol 41:194-200, 1961.

16. Volkova, Z., E. A. Sidorva: [Blood formaldehyde content in persons exposed to the effect of urea-formaldehyde resins.] Gig Tr Prof Zabol 15(5):44-46, 1971 (Russian).

17. Shumilina, A. V.: [Menstrual and child-bearing functions of female workers occupationally exposed to the effects of formaldehyde]. Gig Tr Prof Zabol 75(12):18-21, 1975 (Russian).

18. Schwartz, L.: Dermatitis from synthetic resins and waxes. Am J Public Health 26(6):586-592, 1936.

19. Schwartz, L.: Dermatitis from synthetic resins. J Invest Dermatol 6:239-255, 1945.

20. Markuson, K. E., T. F. Mancuso, J. S. Soet: Dermatitis due to the formaldehyde resins. Ind Med 12(6):383-386, 1943.

21. Grabchak, K. A.: [Prevention of occupational dermatitis caused by urea resins.] Vestn Dermatol Venerol 38:52-54, 1964 (Russian).

22. Karagezyan, M. A., T. N. Zlochevskaya, A. N. Ganzha: [Occupational dermatic diseases in furniture production and their prevention.] Vestn Dermatol Venerol 43:53-58, 1969 (Russian).

23. El-sayad, I. A.: [Effect of formaldehyde resins on the skin.] Gig Tr Prof Zabol 16(8):46-48, 1972 (Russian).

24 Torsuev, N. A., M. N. Bukharovich, N. N. Speranskii, I. Ya. Zakharov, A. F. Molitskii, A. M. Bukharovich: [Occupational skin diseases in workers making glass wool cylinders.] Gig Tr Prof Zabol 3:43-44, 1974 (Russian).

25. Shevlyakov, L. V.: [Course experimental allergic dermatitis caused by urea formaldehyde resins.] Vestn Dermatol Venerol 47:64-66, 1973 (Russian).

26. Chanial, G., D. Duguaire, D. Pernet: [Occupational dermatitis due to preparation (formaldehyde solution and urea) for processing non-crushable fabrics.] Arch Mal Prof 14:65-66, 1953 (French).

27. Moskovtchenko, P.: [Occupational dermatoses in persons working with preparation (formol, solution of formaldehyde, and urea) for processing noncrushable fabrics.] Arch Mal Prof 14:32-35, 1953 (French).

28. Marcussen, P. V.: [Eczema caused by formaldehyde resins coating anti-curl substances.] Ugeskr Laeg 124:237-240, 1962 (Danish).

29. Jakovljevicova, E.: [Professional urticaria caused by urea-formaldehyde resin.] Cesk Dermatol 51(5):323-326, 1976 (Czechoslovakian).

30. Peck, S. M., L. L. Palitz: Sensitization to facial tissues with urea-formaldehyde resin (wet-strength). J Am Med Assoc 160:1226-1227, 1956.

31. Schwartz, L.: Dermatitis from new synthetic resin fabric finishes. J Invest Dermatol 4(6):459-470, 1941.

32. O'Quinn, S. E., C. B. Kennedy: Contact dermatitis due to formaldehyde in clothing textiles. J Am Med Assoc 194:593-596, 1965.

33. Shellow, H., A. T. Altman: Dermatitis from formaldehyde resin textiles. Arch Dermatol 94:799-801, 1966.

34. Marcussen, P. V.: Dermatitis caused by formaldehyde resins in textiles. Dermatologica 125:101-111, 1962.

35. Malten, K. E.: Textile finish contact hypersensitivity. Arch Dermatol 89:215-221, 1964.

36. Fisher, A. A., N. B. Kanof, E. M. Biondi: Free formaldehyde in textiles and paper. Arch Dermatol 86:753-756, 1962.

37. Brodhage, H., A. R. Stofer: Polyoxymethyleneurea, a new type of locally applicable chemotherapeutic agent. Antibiot Chemother 11:205-206, 1961.

38. Galibin, G. P.: [Action of hardened synthetic resins on animal systems.] Toksikol Nov Prom Khim Veshchestv 5:45-50, 1963 (Russian).

39. Anderson, G. C., G. A. McLaren, J. A. Welch, C. D. Campbell, G. S. Smith: Comparative effects of urea, uramite, biuret soybean protein and creatine on digestion and nitrogen metabolism in lambs. J. Anim Sci 18:134-140, 1959.

40. Al'bitskaya, O. N., N. A. Shaposhnikova: [The stability of electrical insulation materials toward attack by mold fungi.] Vestn Elektroprom 30(10):54-59, 1959 (Russian).

41. Haler, D., A. Aebi: A new, highly effective but non-toxic antibacterial substance. Nature 190:734-735, 1961.

42. Haler, D.: Polynoxylin. Nature (London) 198:400-401, 1963.

43. Tomasini, C.: [Clinical experience topical use new preparation derived polycondensation urea formaldehyde (anaflex).] G Ital Dermatol 103:56-61, 1962 (Italian).

44. O'Donnell, J. M.: Sterilized organic waste product and process of producing same. U. S. Patent 3,976,465, 1976.

45. Kingston, D.: Release of formaldehyde from polynoxylin and noxythiolin. J Clin Pathol 18(5):666-667, 1965.

46. DeGrisse, A., F. Moussa, A. Heungens: Nematicidal effect of the soil conditioner hygromull on soil-inhabiting nematodes in comparison with Dupont 1410 and Busan 881. Meded Fac Landbouwwet Rijksuniv Gent 36(4):1365-1374, 1971.

47. Heungens, A.: [Influence of hygromull on the soil fauna in azalea culture.] Meded Fac Landbouwwet Rijksuniv Gent 37(2):824-830, 1972 (Dutch).

48. Fuller, W. H., K. G. Clark: Microbiological studies on urea-formaldehyde preparations. Soil Sci Soc Am, Proc 12:198-202, 1948.

49. Pantosne, T. D., G. Pantos: [The mineralization of ureaform preparations by microorganisms isolated from corn root.] Agro Talajtan 8:313-320, 1959 (Russian).

50. Long, F. L., G. M. Volk: Availability of nitrogen contained in certain condensation products of reaction of urea with formaldehyde. Agron J 55(2):155-158, 1963.

51. Bengtson, G. W., G. K. Voigt: A greenhouse study of relations between nutrient movement and conversion in a sandy soil and the nutrition of slash pine seedlings. Soil Sci Soc Am, Proc 26(6):609-612, 1962.

52. Musser, H. B., J. M. Duich: Response of creeping bentgrass putting-green turf to urea-form compounds and other nitrogenous fertilizers. Agron J 50:381-384, 1958.

53. Waddington, D. V., E. L. Moberg, J. M. Duich, T. L. Watschke: Long-term evaluation of slow-release nitrogen sources on turfgrass. Soil Sci Soc Am J 40(4):593-597, 1976.

54. Prasad, M., M. J. Woods: Release characteristics of nitrogen fertilizers in peat and sand. J Agric Food Chem 19(1):96-98, 1971.

55. Gajbe, M. V., A. B. Ghosh: [Leaching of nitrogen from a soil fertilized with slow-acting urea-aldehyde complexes.] Agrokem Talajtan 25(3-4):297-304, 1976 (Hungarian).

56. Anonymous: Adhesives used in particleboard. Encyclopedia of Polymer Science and Technology, Interscience Publisher, New York, 1964, 4:98-99.

57. Conley, R. T.: Oxidative mechanisms for the degradation of phenol, furan, and urea based condensation polymers. Proc Battelle Symp Thermal Stability Polymers, Columbus, Ohio 1963, 68 pp.

58. American Converence of Governmental Industrial Hygienists: Documentation of the threshold limit value for substances in workroom air, 3rd Edition, 1971.

59. Alexander, A. L., F. M. Noonan, J. E. Cowling: The degradation of polymers by ultraviolet irradiation. Part 1. When subjected to radiation of the "near" ultraviolet region in air. NTIS Publ No 151411, 1975.

60. Vee, J. Y., K. S. Love: Nitrification of urea-formaldehyde reaction products. Soil Sci Soc Am, Proc 11:389-392, 1947.

61. Winsor, G. W., I. E. Long: Mineralization of the nitrogen of urea-formaldehyde compounds in relation to soil pH. J Sci Food Agric 7:560-564, 1956.

62. Hadas, A., U. Kafkafi, A. Peled: Initial release of nitrogen from ureaform under field conditions. Soil Sci Soc Am, Proc 39(6):1103-1105, 1975.

63. Long, M. I. E., G. W. Winsor: Isolation of some urea-formaldehyde compounds and their decomposition in soil. J Sci Food Agric 11:441-445, 1960.

64. Anonymous: Summary of NIOSH recommendations for occupational health standards. Chem Regulation Reporter 1(39): Dec. 9, 1977.

65. Shtromberg, M. S.: [Hygienic evaluation of working conditions and recuperative measures in production of urea-formaldehyde resins.] Gig Sanit 21(7):45-47, 1956 (Russian).

66. Volkova, Z. A., M. V. Aldyreva, N. S. Zlobina: [Occupational hygiene in utilizing polymers as an industrial raw material.] Gig Tr Prof Zabol 10(11):7-12, 1966 (Russian).

67. Dueva, L. A.: [Experimental materials contributing to the establishment of hygienic standards for urea-formaldehyde resins.] Gig Tr Prof Zabol 10:39-43, 1966 (Russian).

68. Grigor'eva, M. N., N. G. Shplet: [Hygienic characteristics of urea plastic foams.] Gig Sanit 7:106-108, 1973 (Russian).

69. Bartenev, V. D., M. E. Son'Kin: [On the hygienic evaluation of synthetic materials used in construction.] Vrach Delo 7:90-93, 1968 (Russian).

70. Kuz'menko, N. M., A. I. Ereslenko, S. E. Kataeva, T. I. Kravchenko, R. S. Asatryan: [Study of sensitizing effect of formaldehyde under conditions in production of plastic masses.] Vrach Delo 6:131-134, 1975 (Russian).

71. Ermolenko, A. E.: [Labor hygiene in the preparation of foundry cores by cold hardening]. Gig Tr Prof Zabol 7:51-52, 1976 (Russian).

72. Pesin, L. M., I. L. Derkovskaya, S. L. Golodnaya, A. N. Pukhovitskaya, E. A. Akopdzhanyan: [The purification of urea resin waste waters from formaldehyde.] Plast Massy 8:58-60, 1964 (Russian).

73. Mikhailova, A. A., E. I. Lifshits, L. T. Ivanova, F. S. Grinberg,
     R. Z. Temkina, G. M. Shvartsman, G. G. Yudina, M. M. Svitkina:
     [Improvement of the sanitary-hygienic properties of chipboards.]
     Gig Sanit 7:86–88, 1974 (Russian).

74. Andersen, Ib., G. R. Lundqvist, L. Molhave: Indoor air pollution
     due to chipboard used as a construction material. Atmos Environ
     9(12):1121–1127, 1975.

75. Baumann, H.: [Formaldehyde in UF foam.] Plastica 30(3):72–74, 1977
     (Dutch).

76. Bloham, S. G.: Formaldehyde contact dermatitis. Acta Derma Venereol
     39:450–453, 1959.

77. Clermont, L. P., M. N. Carroll: Improved chromotropic acid determin-
     ation of formaldehyde evolution from wood composites. For Prod J
     26(8):35–37, 1976.

78. Plath, L.: [Detection and separation of aminoplasts by paper chroma-
     tography.] Adhaesion 5:174, 176, 179–180, 1970 (German).

79. Ludlam, P. R.: Thin-layer chromatography of simple urea-formaldehyde-
     methanol reaction products. Part I. Qualitative Aspects. Analyst
     98:107–115, 1973.

80. Ludlam, P. R.: Thin-layer chromatography of simple urea-formaldehyde-
     methanol reaction products. Part II. Quantitative aspects. Analyst
     98:116–121, 1973.

81. Wise, J. K., C. D. Smith: Infrared spectrometric examination of paper.
     II. Determination of urea-formaldehyde resin. Anal Chem 39(4):1702–
     1705, 967.

82. Horacek, J., Z. Malkas: [Damping of polarographic maxima as one cri-
     terion for the evaluation of plastics.] Nahrung 7(2):173–181, 1963
     (German).

83. Dankelman, W., J. M. H. Daemen, A. J. J. deBreet, J. L. Mulder,
     W. G. B. Huysmans, J. deWit: [Modern methods for the analysis of urea
     formaldehyde resins.] Angew Makromol Chem 54(1):18 201, 1976 (German).

84. Richard, B., A. Gourdenne: [NMR analysis of an urea-formaldehyde
     resin.] Comptes Rendus Acad Sci, Ser C 281(20):815–817, 1975 (French).

85. Sluzewska, L., H. Piekaez: [Hygienic evaluation of plastic materials.
     I. Formaldehyde determination in aminoplasts and phenoplasts.]
     Rocz Panstw Zakl Hig 11(6):557–566, 1960 (Polish).

86. Tsuchiya, K., Y. Hayashi, M. Onodera, T. Hasegawa: Toxicity of
     formaldehyde in experimental animals – concentrations of the chemical
     in the elution from dishes of formaldehyde resin in some vegetables.
     Keio J Med 24:19–37, 1975.

87. Nash, T.: The colorimetric estimation of formaldehyde by means of the Hantzsch reaction. Biochem J 55:416–421, 1953.

88. Harkin, J. M., J. R. Obst, W. F. Lehmann: Visual method for measuring formaldehyde release from resin-bonded boards. For Prod J 24(1):27–30, 1974.

APPENDIX

Information Sources Examined

Computer Searchable Data Bases

1 – National Technical Information Services (searched on Oct. 5, 1977)

2 – Toxline/Toxback (searched on September 20, 1977)

3 – Chemical Condensates (searched on September 27, 1977)

4 – ISI SCISEARCH (searched on Oct. 5, 1977)

5 – Cancerline (searched on October 4, 1977)

6 – NIOSH Technical Information Center file (received on Oct. 11, 1977)

7 – Defense Documentation Center (received on September 25, 1977)

8 – Enviroline (received on Oct. 11, 1977)

9 – Water Resources Scientific Information Center (WRSIC)
     (received on October 6, 1977)

10 – Office of Hazardous Materials/Technical Assistance Data System
      (OHM/TADS) (received on October 6, 1977)

11 – Pollution Abstracts (received on Oct. 11, 1977)

12 – AGRICOLA (received on Oct. 17, 1977).

Hard Bound Secondary References

1. Chemical Abstracts – V. 1 (1907) – V. 75 (1971).

2. Index Medicus – V.1 (1927) – V.18 (No. 4), 1977.

3. Excerpta Medica – sections entitled Toxicology and Pharmacology, Occupational Health and Industrial Medicine, Cancer, Environmental Health and Pollution Control (covering Vol. 1 through last volume available in 1976) were examined.

4. Engineering Index – (covering 1940 through 1977, issue #3).

5. Biological Abstracts – [covering Vol. 1 (1927) through Vol. 64, #6 (1977)].

Other References Examined

1. Gleason, M.N., R.E. Gosselin, H.C. Hodge, R.P.Smith, Clinical Toxicology of Commercial Products, Williams & Wilkins Co., Baltimore, 1976 (Fourth Edition).

2. Browning, E., Toxicity & Metabolism of Industrial Metals, Elsevier Publishing Company, New York, 1965.

3. Goodman, L.S., A. Gilman, The Pharmacological Basis of Therapeutics, The Macmillan Company, New York, 1975 (Fifth Edition).

4. Code of Federal Regulations, July 1, 1976.

5. AIHA hygiene Guide, Cincinnati, American Industrial Hygiene Association.

6. Parke, D.V., Biochemistry of Foreign Compounds, Pergamon Press, Oxford, 1968.

7. Shepard, T.H., Catalog of Teratogenic Agents, The Johns Hopkins University Press, Baltimore, 1973.

8. Fishbein, L., Chromatography of Environmental Hazards, Vol. 1–3, Elsevier Publishing Company, New York, 1973.

9. Thienes, C.L., T.J. Haley, Clinical Toxicology, Lea and Febiger, Philadelphia, 1972 (Fifth Edition).

10. Sax, N.I., Dangerous Properties of Industrial Materials, van Nostrand Reinhold Co., New York, 1975.

11. American Conference of Governmental Industrial Hygienists, Documentation of the Threshold Limit Value for Substances in Workroom Air, 1971 (Third Edition).

12. International Labour Office, Encyclopedia of Occupational Health and Safety, McGraw-Hill Book Co., New York, 1971-1972.

13. The Chemical Society, Foreign Compounds Metabolism in Mammals, Vol. 1 & 2, The Chemical Society, London, 1970 and 1972.

14. Committee on the Handbook of Biological Data, National Academy of sciences, National Research Council, Washington, D.C., Handbook of Toxicology, Vol. 1-5, W.B. Saunders Co., Philadelphia, 1959.

15. World Health Organization, IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, Vol. 1-15, WHO, International Agency for Research on Cancer, Lyon.

16. Patty, F.A. (Ed.), Industrial Hygiene and Toxicology, Interscience Publishers, New York, 1963 (Second Revised Edition).

17. Hamilton, A., E.L. Hardy, Industrial Toxicology, Publishing Sciences Group, Inc., Acton, Mass., 1974 (Third Edition).

18. Kirk-Othmer, Encyclopedia of Chemical Technology, Interscience Publishers, New York, 1972 (Second Edition).

19. Windholz, M. (ed); Merck Index, Merck & Co., Rahway, N.J. 1976 (Ninth Edition).

20. Arena, J.M., Poisoning-Toxicology-Symptoms-Treatments, Charles C. Thomas Publisher, Springfield, Illinois, 1974 (Third Edition)

21 National Institute for Occupational Safety and Health, Registry of Toxic Effects of Chemical Substances, Government Printing Office, Washington, D.C., 1976.

22. National Cancer Institute, Survey of Compounds which have been tested for Carcinogenic Activity, DHEW Publication No. (NIH) 73-453, Rockville, Md., 1973.

23. The International Technical Information Institute, Toxic and Hazardous Industrial Chemicals Safety Manual for Handling and Disposal with Toxicity and Hazard Data, International Technical Information Institute, Tokyo, 1975.

24. National Institute for Occupational Safety and Health, Suspected Carcinogens, Government Printing Office, Washington, D. C., 1976.

25. McKee, J.E., H.W. Wolf (Ed.), Water Quality Criteria, The Resources Agency of California, State Water Resources Control Board, Publication No. 3-A, Reprint June 1, 1976.

26. U.S. Environmental Protection Agency, Quality Criteria for Water, U.S. Environmental Protection Agency, Washington, D. C., Publication No. EPA-440/9-76-023.

27. Murphy, J.S., Municipal Water Pollution Control Abstracts for 1974, Office of Research and Development, U.S. Environmental Protection Agency, Washington, D. C., Publication No. EPA-600/2-75-005, April 1975.

28. Fairhall, L.T., Industrial Toxicology, The Williams & Wilkins Company, Baltimore, Maryland, 1957.

29. Sax, N.I. (Ed.), Industrial Pollution, Van Nostrand Reinhold Company, New York, 1974.

30. Weinstein, L., Teratology and Congenital Malformations, Vol. 1-3, IFI/Plenum Data Company, New York, 1976.

31. Eisler, R., Annotated Bibliography on Biological Effects of Metals in Aquatic Environments (No. 1-567), U.S. Environmental Protection Agency, Corvallis, Oregon, NTIS Publication No. PB 228 211, 1973.

32. Yopp, J.H., W.E. Schmid, R.W. Holst, Determination of Maximum Permissible Levels of Selected Chemicals That Exert Toxic Effects on Plants of Economic Importance in Illinois, Illinois Institute for Environmental Quality, 1974, NTIS Publication No. PB-237 654.

33. Eisler, R., M. Wapner, Second Annotated Bibliography on Biological Effects of Metals on Aquatic Environments, U.S. Environmental Protection Agency, Narragansett, Rhode Island, 1975, NTIS Publication No. PB-248 211.

34. U.S. Environmental Protection Agency, Identification of Organic Compounds in Effluents from Industrial Sources, 1975, NTIS Publication No. PB-241 641.

35. U.S. Environmental Protection Agency, Supplement to Development Document: Hazardous Substances Regulations, Section 311 of the Federal Water Pollution Control Act as amended 1972, NTIS Publication No. PB-258 514, Nov. 1975.

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